The New England
Journal of Medicine
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VOLUME 224 APRIL 17, 1941 NUMBER 16

MYCOTIC INFECTIONS OF THE SKIN*

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THE cutaneous infections discussed in this paper include ringworm of the hands and feet, and several cutaneous conditions formerly classed as separate entities but now known to be due to yeasts or yeastlike micro-organisms.

RINGWORM INFECTIONS

Ringworm of the hands and feet was practically unknown in the United States until 1916, when Ormsby and Mitchell[1] reported a group of 65 patients, in all of whom fungi were demonstrated microscopically. This study included patients suffering with dyshidrosis and intertriginous eczema. Reports of cases had been made previously by Montgomery and Culver[2] (1914), by Hartzell[3] (1915) and by Lane[4] (1916). Some years later, intensive investigative work was instituted; it has been carried on throughout this country until the affection is now accorded a prominent place in the minds of both physicians and the laity. Its importance is undoubtedly exaggerated in the popular mind. The chief criticism at present from the dermatologist's standpoint is that the layman considers practically every cutaneous affection occurring on the feet and hands to be ringworm and treats it accordingly. Unfortunately, numerous physicians fall into the same error, but to a lesser degree. On account of the popular demand for self-treatment, numerous proprietary articles are advertised and extensively sold, some of which inflict much damage. I believe that it is essential that the diagnosis of ringworm be confirmed microscopically in every case before treatment is instituted, and I have done this since the beginning. Unfortunately, many practitioners rely solely on the clinical symptoms for a diagnosis.

Clinical Description

The affection was early described by Whitfield and Kaufmann-Wolf. Each described three clinical types: the acute vesiculobullous, the chronic intertriginous, secondary to the first type, and the chronic hyperkeratotic. In our original investigation we were able to confirm these findings. The initial lesions are vesicles and may be single, multiple, grouped or widely distributed. The vesicles are deep seated, slightly elevated or level with the surface and resemble boiled sago grains imbedded in the epidermis — this comparison is always made in so-called "dyshidrosis." The content of the vesicle is serous unless contaminated by secondary infection. As a rule the early vesicles are not surrounded by redness. After several days to a week, the fluid is absorbed, and a brown macule remains. After desiccation, the roof of the vesicle becomes torn, exposing a red, smooth, shining surface surrounded by a collaret of scales. Sometimes the roof of the vesicle, instead of scaling, develops into a brown keratotic button 1 to 2 mm. thick. Beneath these keratotic lesions the usual red, shining surface is not found. It is through the multiplication of this type of lesion that the hyperkeratotic variety of the disease is produced. In acute cases the vesicles may be grouped, may become confluent and may form bullae. In extensive bullous cases the patients may be incapacitated for weeks. At times well-defined, shiny-red, circular areas, denuded of the corneal layer through desiccation and desquamation of groups of vesicles, develop in dry areas, such as in the center of the palm or on the sole or the arch of the foot. These patches may heal spontaneously, or new vesicles may continue to form around the periphery, with extension in one or several directions. The grouped vesicles may develop into a dry or moist, well-defined, eczematous area. In order of frequency of occurrence, the affected areas are the fourth interspace of the foot, the plantar surface of the arch and the tuberosity of the fifth metatarsus. At the base of the fifth toe, a fissure occupying both the interdigital and plantar areas is commonly present. Occasionally, similar fissures occur in the flexor folds of all the toes. In the fourth interspace, a white,

*Presented at the New England Postgraduate Assembly, Cambridge, Massachusetts, November 13, 1940.

Portions of this paper have been published in the following journals: *Medical Record and Annals* (29:659-664, 1935); *Peoria Medical News* (6:3, 1935); *Journal Lancet* (55:295-301, 1935); and *Journal of the Michigan State Medical Society* (37:135-140, 1938).

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sodden, thickened, adherent mass of epidermis is of common occurrence and is produced through maceration of the exfoliated epidermis. This condition occasionally extends to other interspaces. In the keratotic variety, areas of keratoderma are formed, usually symmetrically and oftener on the soles. Occasionally, a diffuse palmar and plantar keratoderma develops. One of the cases studied in our original investigation had had symmetrical palmar and plantar keratoderma for thirty-two years. When the disease is complicated by secondary infection, there is often much swelling and edema of the undersurface of the toes, the contiguous portion of the soles and the intertriginous surface of the toes. Under these circumstances much tenderness and pain is experienced.

Ordinarily the chief subjective symptom is itching, which may be moderate to severe but is practically always present. In the widespread acute bullous cases, as well as those complicated with secondary infection, sensitiveness and pain are characteristic. Although in most cases the eruptive manifestations are limited to the feet and hands, occasionally well-defined, scaling patches of dermatitis may occur over the trunk and limbs, and in these the causative fungus can be found.

Diagnosis

The major portion of cases of dyshidrosis are examples of ringworm, like a great many cases formerly classed as intertriginous eczema, together with a certain percentage of cases of localized keratoderma of the hands and feet. An immediate diagnosis can nearly always be made by a microscopic examination of the roof of a sago-grain vesicle or of scales taken from the interdigital spaces, as well as from other scaling areas on the foot. The material to be examined is placed on a slide in a drop of a 10 to 20 per cent solution of sodium hydroxide. If the roof of the vesicle is used, it is placed with its undersurface up, the cover slip is placed over the preparation and the slide is gently heated until the preparation boils. Examination with a medium-powered lens reveals the fungus, which is seen as jointed mycelial filaments.

Disorders from which ringworm is to be distinguished are dyshidrosis, eczema, a resistant vesicular dermatitis of the palms and soles, a superficial vesicular eruption probably of infectious origin, an external irritant dermatitis and a pustular eruption of the palms and soles described below. Although the major portion of cases of what were formerly considered dyshidrosis are examples of ringworm, there still remain a number that can be regarded as dyshidrosis; these patients usually present a constitutional background, indicated by circulatory changes, excessive sweating and so forth. In the resistant vesicular dermatitis, which is probably of toxic origin, the vesicles are usually deep seated, limited to the palms and soles, and do not involve the intertriginous areas. In practically all the cases that I have seen, the affection has been considered ringworm and treated as such without beneficial results. In the superficial vesicular type of infectious origin, similar areas of dermatitis may be observed on the glabrous skin; this finding is of diagnostic importance. In the external irritant type, the lesions are apt to be between the fingers and on the dorsum rather than on the palmar surface. In none of these is the ringworm fungus found microscopically.

Ringworm is readily distinguished from a pustular infection occurring on the palms and soles that has been described by Barber[5] as pustular psoriasis, by Audry[6] as an abortive form of *acrodermatitis continue*, and by Andrews, Birkman and Kelly[7] as a recalcitrant pustular eruption of the palms and soles. This lesion is characterized by an exfoliative type of dermatitis beginning in the center of the palms, extending over the thenar and hypothenar eminences and at times covering the entire palm and palmar surface of the fingers. On the feet it occurs characteristically on the insteps, from which it may spread over the entire plantar surface. The interdigital areas, usually invaded by ringworm, are free. The early lesion is a small flat discrete pustule. Throughout the patch there are scattered pustules and crusts. These are more abundant at the margins. The course of the affection is characterized by periods of activity and partial quiescence. During the former, severe burning sensations occur. The lesions are resistant to treatment, and microscopic examination reveals no fungi.

Absence of fungi in the vesicles or scales taken from the feet is important from a diagnostic standpoint. It is much less significant in similar lesions taken from the palms. This is explained, as noted elsewhere, on the ground that in numerous cases of ringworm infection the palmar lesions are so-called "ide" eruptions, in which micro-organisms are rarely found.

Etiology

Men are affected oftener than women, and the cases have usually been diagnosed as dyshidrosis or eczema. The feet are affected much more frequently than the hands. Eczema marginatum not infrequently precedes the infection. Familial transmission occurs. Infection is more prevalent in warm weather, exacerbations occurring in the spring and autumn, but sporadic cases do occur during the winter months.

Various members of the genera, Epidermophyton and Trichophyton, are responsible for the affection. These organisms may lie dormant for long periods in calluses, under or about the nail or even in the superficial layers of epidermis between the toes. From these points reinfection occurs when heat and moisture develop in the warm season. Common sources of infection are dressing rooms, runways and shower baths in the athletic departments of schools and universities and in athletic and country clubs. The prevalence of mycotic infection of the feet and its increase in the gymnasiums of universities are well shown by a report by Legge, Bonar and Templeton[8] from the University of California. At the beginning of the fall gymnasium work, 3105 freshman matriculants were examined; 51.5 per cent of the men showed clinical evidence of ringworm of the feet. At the end of the semester the same medical examiners found the proportion of involvement to be 78.6 per cent, an increase of 27 per cent. The infection was present in 15 per cent of woman matriculants at the beginning of the semester, and this had increased only 2 per cent at the end of that semester.

Treatment

The method of treatment depends on the type of eruption. When the eruption on the feet is acute, accompanied by vesicles and bullae together with secondary infection, hot soaks with a 1:2000 solution of potassium permanganate used two or three times daily are efficacious. In the interim between soaks, soothing ointments containing naftalan or ichthyol or both may be employed. The following formula is useful:

Naftalan	10
Powdered starch	25
Zinc oxide	25
Petrolatum	*q. s. ad* 100

Ichthyol (2 per cent) may be substituted for naftalan. When the acute stages have subsided, an ointment containing salicylic acid and benzoic acid, originally recommended by Whitfield, is efficient:

Salicylic acid	2
Benzoic acid	4
Petrolatum	*q. s. ad* 30

In our early work we used this or a 10 per cent chrysarobin ointment or suspension.

These preparations cause exfoliation. When this is complete, Hebra's unguentum diachylon alba may be employed at night, with a drying dusting powder containing magnesium carbonate in the morning. The formula for the latter is as follows:

Magnesium carbonate	4
Boric acid	4
Powdered talc	*q. s. ad* 30

This should be continued for several weeks, during which the salicylic acid and benzoic acid ointment mentioned above should be continuously employed as a prophylactic measure around and beneath the nails, and on calluses, if present. In the subacute and keratotic cases, the keratolytic ointment is advisable from the beginning. In the chronic intertriginous type, curettage, employed when the leathery whitened mass has been softened, hastens recovery. On the hands a zinc oxide and lime water lotion is advisable in the vesicular cases, together with the keratolytic ointment suggested for the feet, but reduced 50 per cent in strength. The formula for the lotion is as follows:

Sodium biborate	10
Zinc oxide	15
Powdered starch	15
Lime water	120
Rose water	*q. s. ad* 240

If the lesions are merely dry and scaling, the ointment will be sufficient.

In certain cases injections of trichophytin may be required. These should be used with caution, the initial doses should be small, and perhaps this method should be reserved for resistant and intractable cases.

Prophylaxis

Prevention on a large scale was practiced by Osborne and Hitchcock[9] in the high schools of Buffalo. Through experimental work they demonstrated the efficiency of sodium hypochlorite as a preventive measure. They recommend the employment of rubber pans approximately two feet square containing a 1 per cent solution of sodium hypochlorite. These pans are placed in the shower rooms, and the students immerse the feet in one as they go into the bath and into another as they come out. In new athletic departments, wells are built in the floor of the corridor through which the students pass from the dressing room to the shower baths. The disease in the high schools in Buffalo was reduced to a minimum through these measures.

Sterilization of the shoes, socks and other articles of clothing, together with rugs and carpets that have been in contact with the feet of an infected patient, may be accomplished by formaldehyde fumigation. Ayres, Anderson and Youngblood[10] recommend that this method be employed in the bedroom and bathroom of the affected patient. By the use of fumigation with a formaldehyde candle they demonstrated the effectiveness of

this procedure. Individual prophylaxis in country clubs is promoted by the use of wooden-soled sandals between the locker room and shower.

Epidermophytids

These are eruptions produced by the local action of fungi brought to the skin by way of the blood stream from existing foci. The fungi are immediately destroyed on account of the existing allergy. They may also be secondary to infection of the hands and in the crotch. The ringworm microorganisms are rarely present.

Ordinarily, the eruptions occur in association with acute and severe attacks of ringworm of the feet. Under these circumstances, the secondary eruption has acute manifestations and runs its course in a short time. In other cases, when the primary focus presents practically no recognizable symptoms, the secondary eruption may be of longer duration. The hands are the commonest site of this eruption, and the lesions may be vesicular or squamous. The vesicles may be superficial or deep, and the degree of the accompanying inflammatory reaction may vary. Occasionally, a more widespread eruption, occurring over the forearms, legs and elsewhere, may resemble pityriasis rosea or multiform erythema. Patches of dermatitis resembling eczema occasionally occur, and in rare cases the eruption may resemble a generalized exfoliative dermatitis.

Microscopic examination of the secondary lesion reveals no micro-organisms, whereas they may be demonstrated abundantly in the primary infection on the feet. An excellent experimental confirmation of these lesions was made by Peck,[11] who produced a ringworm infection of the feet in a human subject by inoculation with *Trichophyton gypseum*, which was followed after twenty-four days by a vesicular dyshidrotic type of eruption on the hands. The fungi were readily demonstrable in the primary infection on the feet, but the secondary eruption on the hands was free from organisms and was considered to be an epidermophytid.

Epidermophytids may be distinguished from the eruptions that they resemble by the location of the lesions and the accompanying ringworm infection present on the feet. The trichophytin reaction is positive and is a confirmatory finding. When the secondary eruption is eczematous, the trichophytin test is made by the patch method.

Yeast Dermatoses (Moniliasis)

Clinical Description

A number of cutaneous and mucous-membrane infections formerly described as entities have been found to be due to yeast or yeastlike micro-organisms.[12] Two or more or all these eruptions may coexist in a given patient. Through experimental work all have been produced by inoculation of cultures taken from patients exhibiting the various types of dermatitis.

Paronychia. Mycotic paronychia presents a characteristic picture and has two forms, acute and chronic. The acute form occurs frequently in workers in fruit canneries and in other industrial laborers. The chronic form presents a typical appearance, described by MacLeod[13] as a "pad or bolsterlike swelling of the nail wall, which on being squeezed emits a bead of pus on the nail plate." This enlargement is most marked at the base of the nail and gradually tapers down on the sides toward the distal end of the nail plate. The degree of inflammation varies in different cases, and there is usually an associated dystrophy of the nail plate, owing to interference with the formation of the nail at the lunula. In acute cases, such as those described by Kingery and Thienes,[14] seen in workers in fruit canneries, there is much swelling and pain, and often shedding of the nail.

Onychia. This monilial infection resembles the ringworm type. In the chronic form transverse ridges occur in the nail plate, which becomes opaque, thickened, discolored and brittle. Subungual keratoses are present beneath the lateral and distal portions of the plate, causing it to be raised from the bed.

Perlèche. In this condition, an inflammatory reaction occurs at the angles of the mouth, usually in children.[15] It is characterized by a thickening and whitening of the epithelium, together with fissures. The infection sometimes spreads toward the center of the lip and over the glabrous skin in the immediate vicinity. The thickened epithelium, often likened to mother of pearl, is sometimes easily detached. Occasionally, a moderate degree of crusting occurs. The fissures are superficial and rarely bleed, and ulceration does not occur. A scaling dermatitis of seborrheic type sometimes occurs in the immediate vicinity.

Erosio-interdigitalis. This lesion occurs on the web of the fingers, usually in the third and fourth interspace.[16] It may occupy all the interspaces, and it sometimes occurs between the toes. It is characterized by a shiny red area, surrounded by a collaret of scales; it may also be represented by an accumulated mass of sodden, moist, whitened epidermis. Vesicles are usually absent, although points on the reddened area may indicate former vesiculation. This form of moniliasis is exceedingly difficult to eradicate. In addition to the erosio type of lesion, a vesicular and papulo-

vesicular eruption occurs in the interdigital surfaces, with occasional maceration and fissuring.

Water-bed mycosis. This infection is characterized by the presence of herpetic-appearing vesicles with red areolas, together with pustules.[17] These develop in a continuous water bath or on areas of the skin where moist dressings are applied for a long time. A frequent site is the abdomen, following laparotomy, when moist hot dressings have been employed. At times, when the inflammatory reaction becomes marked, redness, edema, weeping and crusting occur.

Glabrous-skin infections. On the glabrous skin a mycotic dermatitis is characterized by variously sized, well-defined, circular, red, scaling patches. By fusion, gyrate configurations are produced. Moist crusting patches, suggesting eczema, occasionally develop, and in widespread cases there occurs simply a dry dull-red scaling dermatitis. Patches begin with vesicles or vesicopustules, which rupture, leaving denuded red areas surrounded by rings of detached epidermis. These spread peripherally and by coalescence with others form the patches. New vesicles in the vicinity, which develop and undergo the above evolution, result in the invasion of large areas. In the crotch and beneath the breasts and in other intertriginous regions, the bottom of the cleft is usually fissured, and the skin in the involved area is shiny, light to dark red, presents some moisture and has scale-covered margins that are polycyclic in outline. When the anogenital region is involved, varying degrees of itching occur, for the relief of which scratching is practiced; this results in thickening, excoriations and fissuring of the skin. In the anal region the erosio type seen between the fingers is sometimes present.

Patches of dermatitis characterized by redness and vesiculation, scaling and crusting may also be found on the dorsum of the hands and on the forearms. Involvement of these areas frequently occurs in association with the paronychia seen in workers in fruit canneries.

Dermatitis seborrhoeica. The clinical description of this form of dermatitis will not be outlined, since it is familiar to all. The point of interest in this connection is the fact that a yeastlike organism — the pityrosporon of Malassez — was cultivated by MacLeod and Dowling[18] from all types of this affection, and the disorder was reproduced by experimental inoculation. In their work they found it necessary to inject the cultures intradermally, or to rub them into lightly scarified areas, to reproduce the lesions.

Mucous-membrane infections. In addition to thrush, which has long been known to be of mycotic origin, other forms of stomatitis and glossitis occur. Since there is no symptom complex characteristic of monilial infection, and since these organisms are sometimes found as saprophytes in such diseases as syphilis, some difficulty is encountered in recognizing the infections.

On the lip and buccal mucosa and on the mucous membrane of the pharynx and larynx, grayish-white membranous pellicles of varying dimensions are seen. These pellicles are translucent and usually easily detachable. They also occur on the tongue and gums. When the pellicles become more adherent, there is apparently more thickening, and when detached there are superficial erosions, presenting a clinical picture of leukoplakia.

On the buccal mucosa Engman and Weiss[19] early described a lesion that occurred as a glistening white mat of filiform projections situated on a white macerated base.

On the tongue, Zeisler[20] described scroll-like patterns resembling geographic tongue. Robinson and Moss[21] observed an acute form in which the anterior surface of the tongue was red and the papillae were edematous and eroded; they also noted a chronic form in which the papillae were absent and the surface of the tongue presented a smooth or slippery appearance like wet, red rubber. Miller and Morrow[22] described a deep form in which a gummalike lesion developed in the soft palate in the tonsillar region. This lesion developed acutely and caused perforation of the soft palate.

Etiology

Cutaneous and mucous-membrane mycotic infections may occur at any age and in both sexes. Paronychia is at times an occupational disease induced in cases described by Kingery and Thienes[14] by contact with fruit juices in cannery workers, and in the cases described by Sutherland-Campbell[23] by contact with orange juice. It frequently occurs in women who handle sugar, such as those employed in confectionery factories, and in pastry cooks. Diabetes is occasionally a predisposing factor. In the erosio type, constant immersion of the hands in water, a condition imposed in washerwomen, is effective, and constant wet dressings constitute the predisposing factor in the waterbed type. Infection of the skin in infants frequently comes from oral and intestinal thrush, and in adults not infrequently from the stools. The organism most frequently found is *Monilia albicans (Oidium albicans).* Cryptococci, the pityrosporon of Malassez and other yeastlike organisms are also concerned in the production of these mycoses.

Diagnosis

The major portion of cases of mycotic infection of the skin due to monilia and related organisms present sufficiently characteristic symptoms to be recognized. A microscopic examination in all cases is essential. Scrapings from the lesions are mounted on a slide in a 10 to 25 per cent solution of sodium hydroxide, over which a cover slip is applied, and the preparation is gently heated. The organism shows plainly and presents the following characteristics with a medium high-power objective: mycelium and sporelike bodies are seen; the myceliums are more delicate and less refractile than those of the ringworm fungi, and septums are rarely demonstrable; oval sporelike bodies, with buds attached to the ends, are also present. In young cultures the organism appears chiefly as round or oval cells, which multiply by budding; in old cultures hyphae develop.

Treatment

Oral thrush in infants responds well to swabbings with a 1 per cent solution of gentian violet, together with mild alkaline mouth washes. For superficial lesions of the mucous membranes of the mouth and vagina, a 3 per cent solution of gentian violet used on a swab twice daily, is efficient. Alkaline mouth washes for the oral cavity and a douche containing a 1:2000 solution of potassium permanganate for the vagina facilitate recovery. For the deeper lesions on the oral mucosa surgical excision, roentgen rays and potassium iodide internally may be necessary.

Paronychia responds quickly to local applications of a 5 per cent suspension of chrysarobin in chloroform. This was originally recommended by Morrow and Lee[24] for the treatment of chronic paronychia, before moniliasis had been recognized. In the erosio type, which is resistant, the parts should be kept dry. The local application of a 5 to 10 per cent solution of chrysarobin or tincture of iodine is valuable. In the water-bed type, the suspension of wet dressings, together with the application of zinc oxide and lime water lotion, and the 10 per cent naftalan or 2 per cent ichthyol ointment previously described, soon relieves the condition.

In the intertriginous type, occurring especially beneath the breasts and in the crotch, painting with a 3 per cent solution of gentian violet is very efficacious. When much inflammatory reaction is present, a preliminary treatment for several days may consist in soaking the parts twice daily with a hot 1:2000 solution of potassium permanganate, dressing the parts in the interim with the naftalan ointment previously mentioned.

In perlèche, Finnerud[15] found the local application of an 8 per cent solution of silver nitrate to be effective. This application may be repeated at intervals of three or four days. Prophylaxis, necessary when this condition occurs in epidemics, consists in the use of individual drinking cups and towels, careful sterilization of the utensils used by the patients, and the avoiding of direct contact.

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THE DEVELOPMENT OF THE CONCEPT OF HYPERTENSIVE HEART DISEASE

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GENERAL recognition of the importance of hypertensive heart disease is comparatively recent. Yet more than a century ago physicians were familiar with cardiac hypertrophy unassociated with valvulitis or heart failure, and they devoted considerable discussion to its clinical and post-mortem features. In 1930, Weiss[1] traced the historical development of the concept of essential hypertension, but since his study did not deal primarily with the hypertensive heart, a review of this aspect of the problem is of interest.

Corvisart[2] in 1812 presented a list of factors of possible significance in the production of cardiac hypertrophy not due to valvular disease, but it remained for Bertin,[3] about twenty years later, to investigate their relative importance. Bertin appreciated the importance of mechanical obstruction as a cause of hypertrophy, but was unable to explain all forms of cardiac enlargement on this basis. Consequently he proposed the theory that cardiac hypertrophy was due to the "irritating" stimulus of an increased quantity of arterial blood in the chambers of the heart.

Hope,[4] his English contemporary, however, maintained that cardiac hypertrophy could be explained on the basis of mechanical obstruction alone. In his textbook, published in 1832, he speaks of the effects of a "preternatural" pressure of blood on the heart.

> According to the foregoing opinons on the mode of formation of hypertrophy, it will be apparent that every circumstance capable of increasing the action of the heart for a sufficient length of time may be a cause of hypertrophy. These circumstances may be either, first, of a nervous or, second, of a mechanical nature.
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> The latter class embraces all physical causes which can either accelerate or obstruct the circulation, and thus occasion a preternatural pressure of blood upon the heart.
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> The physical causes which obstruct the circulation are very numerous. They comprise smallness of the aorta, whether congenital or acquired; dilatation of the aorta; inequalities of its internal surface; all diseases of the valves of the heart which either contract their apertures or impede their movement; adhesion of the pericardium; all affections of the chest that obstruct the circulation through the lungs; as peripneumony, acute, or chronic; empyema, hydrothorax; chronic catarrh; emphysema. . . . As an obstacle of the circulation operates on the heart in a retrograde direction, the cavity situated immediately behind it is the first to suffer from its influence. Accordingly all the impediments seated in the aorta, its mouth or the arterial system, act primarily on the left ventricle, which, being likewise exposed to the heaviest burden when the circulation is accelerated, has to conflict against a greater variety of exciting causes of hypertrophy, than any other cavity of the heart.

Other writings of this period also give the impression that the existence of an extracardiac factor in the causation of hypertrophy was suspected; the two observations that did most to nurture this suspicion were the frequent association of apoplexy and enlargement of the left ventricle, and Bright's discovery of the association of kidney disease and cardiac hypertrophy. The following statements by Bertin[3] and by Hope[4] indicate how well the first observation was appreciated:

> Nothing is better demonstrated in physiology, in the present day, than the influence of the left heart on the circulation of the encephalon; we might, consequently, advance *a priori* that one of the immediate consequences of hypertrophy of the left ventricle would be a predisposition to apoplexy, to encephalitis, and, in fact, to all the cerebral irritations.
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> Since the researches of the present day have demonstrated that even a slight thickening of the walls of the heart constitutes a morbid state; and have unfolded to view the connection subsisting between that state and a train of symptoms formerly either wholly overlooked or attributed to other causes; instances of apoplexy supervening upon hypertrophy have been so frequently noticed, that the relation of the two as cause and effect is one of the best established doctrines of modern pathology.

Perhaps more important was the observation by Bright[5] in 1836 that cardiac hypertrophy was frequently associated with contracted kidneys. In his paper, entitled "The Tabular View of the Morbid Appearance in 100 Cases Connected with Albuminous Urine," he established conclusively that there is a relation between kidney disease and cardiac hypertrophy.

> The first circumstance which strikes the mind, is the extent and frequency to which the derangement of one organ is connected with the derangement of several others; yet we are not at liberty to assume that the disease of the kidney has been the primary cause on which the depression of the rest depended. It may be that some other organ has first suffered, and that the

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> kidneys, together with the rest, have become involved. . . . I am inclined to believe that the kidney is the chief promoter of the other derangements. . . . The obvious structural changes in the heart have consisted chiefly of hypertrophy with or without valvular disease; and what is most striking, out of fifty-two cases of hypertrophy, no valvular disease whatsoever could be detected in thirty-four; but in eleven of these thirty-four, more or less disease existed in the coats of the aorta; still, however, leaving twenty-two without any probable organic cause for the marked hypertrophy generally affecting the left ventricle. This naturally leads us to look for some less local cause, for the unusual efforts to which the heart has been impelled, and the two most ready solutions appear to be, either that the altered quality of the blood affords irregular and unwonted stimulus to the organ immediately; or, that it so affects the minute and capillary circulation, as to render greater action necessary to force the blood through the distant sub-divisions of the vascular system.

Although the clinicians of this period were familiar with nonvalvular hypertrophy as a clinical and pathological entity, they did not clearly understand its relation to cardiac failure. Bertin, for example, contended that it had nothing to do with the signs and symptoms of heart failure, that these were due to other cardiac changes such as valvular lesions, and that uncomplicated cardiac hypertrophy was characterized by evidence of increased cardiac activity and energy of the circulation rather than by signs of failure. To this, Hope also took exception. He agreed that it might be true of the pure uncomplicated form of cardiac hypertrophy, before embarrassment of the circulation had occurred, but not later:

> . . . the truth I believe to be, that the very same energy of the circulation which gives rise to active hemorrhage, apoplexy, etc., causes, as its next effect, engorgement of the arterial capillary system; the necessary consequence of which is serous infiltration and more or less of all the other symptoms indicative of retardation of the circulation.

Thus Hope pointed out a connection between nonvalvular cardiac hypertrophy and heart failure, but he had little understanding of the nature of heart failure, believing as he did that it was a consequence of the effects of hypertrophy on the peripheral capillary system. A clear description of the nature of heart failure did not appear until the writings of Bamberger[6] in 1857.

Bright's conception of renal disease as the primary focus of a general disturbance stimulated further observation that finally led to the recognition of the following separate clinical entities: essential hypertension, diffuse atherosclerosis and primary renal disease with hypertension. Wilks,[7] in 1852, called attention to the occurrence of thickened and tortuous arteries in Bright's disease, and also pointed out that albuminuria was not invariably present. He thus raised the possibility that other conditions might precede the loss of kidney function. At this time Johnson[8] held that it was the small vessels of the body, including even those of the skin, that were contracted and thickened in nephritis. He proposed the thesis that the toxic blood was unable to nourish the tissues; that the minute arteries resisted the passage of this toxic blood and that, as a result of this resistance, both cardiac and arterial muscle tissue became hypertrophied. Traube[9] also maintained that in renal disease an increased resistance to renal blood flow resulted in an abnormal tension in the aortic system and hypertrophy of the left ventricle. In his discussion of kidney disease, Traube states:

> I believe that the cause for the increase in aortic tension is the abnormal resistance which results from the inflammation of the kidneys and which obstructs the outflow of blood from the aorta through the vessels of the kidney. . . . This increase in tension in the aortic system caused by the decrease in the outflow of blood from the aorta, is itself the cause of left ventricular hypertrophy. . . .

Both Johnson and Traube agreed with Bright that the cardiac and vascular changes were secondary to the primary disturbance of kidney function.

The next important contribution to the subject was that of Gull and Sutton[10] in 1872. After an exhaustive study, they concluded that there was a primary disease of the vascular system throughout the body characterized by a diffuse hyaline fibrosis, and that this condition was independent of renal disease. Their proof that marked cardiac hypertrophy and widespread capillary fibrosis could exist with varying degrees of nephritis stimulated the search for factors other than kidney disease as the cause of the cardiac hypertrophy. Further progress in the differentiation of hypertensive states had to await the development of clinical instruments for the measurement of blood pressures.

Mahomed,[11, 12] using a crude method for determining blood pressures, pointed out for the first time in 1874 that there was a condition in which the blood pressure was elevated before there was any albuminuria or evidence of renal disease. He also attached great importance to the circulatory system in the origin of this disease, and maintained that the disease in the arterial system was really the cause of the albuminuria, rather than that the albuminuria was the cause of the vascular fibrosis.

Von Basch[13] soon showed that elevated blood pressures were common, and with the aid of more precise instruments he accumulated measurements and observations that have formed the basis of the modern concept of essential hypertension. He also

observed that the blood pressure may be normal or elevated in severe circulatory failure, and that although palpation of the larger arteries may reveal no evidence of arteriosclerosis, the smaller vessels may be the site of considerable change. On the other hand, he did not understand the relation between hypertension and arteriosclerosis, for he believed that the blood pressure was invariably high in the presence of arteriosclerosis and that it was an accurate clinical index of arterial disease.

The clinical state of hypertension then drew the attention of physicians, including Huchard,[14] Sawada,[15] Allbutt[16] and Pal.[17] Huchard did not carefully distinguish between diffuse arteriosclerosis, as such, and essential hypertension, but Sawada, in 1904, demonstrated that the blood pressure was often normal in the presence of extensive arteriosclerosis. Influenced by this observation and by Mahomed's concept, Allbutt fostered the theory that hypertension was an independent condition. He clearly differentiated arteriosclerosis of the larger vessels from arterial hypertension or, as he called it, "hyperpiesia." Volhard and Fahr[18] reinvestigated kidney diseases in 1914 and differentiated vascular nephrosclerosis from primary renal disease. Primary hypertension, however, was not considered a separate clinical condition for a long time, although a few outstanding clinicians advocated this new concept.

While these relations were being clarified, the condition of the heart in patients with elevated blood pressures received increasing attention. Allbutt did much to crystallize the thought that hypertensive heart disease was a distinct clinical entity, with a course differing from that in nonhypertensive cases. He believed that the hypertensive heart failed when the strength of its hypertrophied muscle fibers was exhausted, and that after a certain degree of hypertrophy the heart had little capacity for recovery. Krehl[19] and Huchard,[14] on the other hand, stressed the importance of cardiosclerosis or disease of the coronary arteries in the production of this type of heart failure. In this country, Fahr[20] was one of the first to appreciate the clinical significance of hypertensive heart disease. He maintained that heart failure unassociated with chronic valvular disease was most frequently of this origin. Christian[21] also stressed the importance of this form of heart disease.

In 1928, Bell and Clawson[22] pointed out the high incidence of coronary sclerosis in hypertensive patients, and Levine and Brown[23] called attention to the frequency of hypertension in patients with coronary thrombosis. Murphy, Grill, Pessin and Moxon,[24] studying the same problem, found that more than 25 per cent of their cases of hypertensive heart failure had gross coronary involvement. Thus, it became established that hypertensive heart disease was associated not only with cardiac hypertrophy but also with an increased incidence of coronary atherosclerosis.

Difference of opinion, however, concerning the relative importance of these factors still prevailed. We reinvestigated the problem, by comparing the anatomical findings in hypertensive and nonhypertensive patients with angina pectoris and congestive failure, and found that both angina pectoris and congestive failure occurred with less coronary sclerosis in hypertensive patients.[25, 26] Severe coronary disease, with occlusion of one or more vessels, was present in 90 per cent of normotensive patients with angina pectoris, whereas in the hypertensive group, coronary disease of this magnitude was present in only 55 per cent. A corresponding difference in the incidence of myocardial infarction in both groups was also demonstrated. Likewise, in patients with congestive failure, severe coronary disease was invariably present in the nonhypertensive cases, but was found in only 53 per cent of the hypertensive group. It appeared established, therefore, that factors other than coronary disease are also important in the mechanism of both angina pectoris and congestive failure associated with hypertension. Two factors known to be present in this condition are cardiac hypertrophy and increased cardiac work.

It has been suggested that cardiac hypertrophy interferes with nutrition of the heart muscle, because the number of capillaries remains unchanged in spite of the increase in muscle mass[27] and because oxygen diffusion is impaired in the hypertrophied muscle fibers.[28] Increased cardiac work is known to be important in angina pectoris associated with thyrotoxicosis and anemia. These two factors are present in most patients with hypertension, and their relative importance is probably related to the magnitude of the hypertrophy and the degree of hypertension present.

Since it was first demonstrated that atherosclerosis was increased in essential hypertension, many have held that atherosclerosis is due to the effects of the elevated tension on the walls of the arterial system. This concept appeared to be in harmony with the increased occurrence of atherosclerosis with age. Our[29] studies, however, have shown that the atherosclerosis found in patients with essential hypertension is unrelated to the elevated tension itself. The coronary arteries of patients with marked hypertension of renal origin, for example, did not show the increased incidence of atherosclerosis found in patients with essential hypertension. In patients with renal hypertension,

the degree of coronary sclerosis was the same as that in controls of the same age and sex. Likewise no relation was found between the severity of hypertension — as evidenced by blood-pressure levels and heart weights — and the degree of coronary sclerosis. These findings are in harmony with the experimental studies of Goldblatt,[30] who observed no increased atherosclerosis in his dogs in which experimental hypertension was induced.

* * *

It appears, then, that in the pathogenesis of hypertensive heart disease there are two coincidental yet independent phenomena. The first is the development of elevated blood-pressure levels that in time lead to cardiac hypertrophy and increased cardiac work, both of which demand additional nourishment for the myocardium. The second is the increased tendency toward atherosclerosis, especially of the coronary vessels, which interferes with cardiac nourishment and function.

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PULMONARY FIBROSIS IN RAYNAUD'S DISEASE*

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RAYNAUD'S disease is usually defined as an intermittent spasm of the digital arteries brought on most frequently by exposure to cold or by emotional strain. It is always symmetrical in its manifestations.

The disease is not always confined to the digital arteries. Cases of Raynaud's disease have been reported in which intermittent blindness as well as transient hemiplegias occurred, presumably due respectively to spasm of the retinal and cerebral vessels.[1] As Raynaud's disease progresses, nutritional disturbances of the skin, manifested by fibrosis, take place. These sclerodermatous changes are not confined to the hands, but may frequently involve the skin of the ears, nose and face.

The manifestation of nutritional skin changes and fibrosis over areas other than the skin of the fingers makes it seem probable that the vasospasm that causes Raynaud's phenomenon may also occur in the small arteries of the skin. The absence of acute circulatory phenomena in the skin may be due to the greater anastomosing circulation in the skin as compared with that in the digital arteries. However, when alterations in the walls of the small vessels take place and there is a permanently insufficient blood supply to the skin, the normal skin degenerates and is replaced by connective tissue.

The question naturally arises whether the same nutritional and subsequent fibrotic changes in the skin may not also occur in other organs of the body secondary to vascular changes similar to those in the digital arteries.

The following cases started with the typical phenomenon of Raynaud's disease, developed sclero-

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derma and showed pulmonary fibrosis in the absence of any other known etiologic factor. The fibrosis of the lungs ran a course much more rapidly progressive than is usually seen in other types of pneumofibrosis.

Case Reports

Case 1. Mrs. S. A., a 45-year-old woman, had noted for about 12 years that on exposure to cold the middle fingers of both hands became dead white, then cyanotic and then red. This was associated with painful tingling and numbness of the finger tips. The attacks increased in frequency and severity, and after about 5 years the skin of the fingers and hands became permanently cyanotic and hard; the fingers could not be fully extended, the terminal phalanges were narrow and shortened, and the nails were curved because of atrophy of the finger pulps. These sclerodermatous changes later involved the skin of the face, which became smooth, firm, somewhat expressionless and diffusely pigmented. The feet were affected to a slighter degree. All arterial pulsations could be felt, in both the hands and the feet.

About 10 years after the onset of the disease, during an examination because of a mild upper respiratory infection, dullness, accompanied by numerous fine crackling rales, at the base of the left lung was found. The breath sounds were bronchovesicular, and there was increased fremitus to the spoken and whispered voice. The heart was displaced to the left. These signs had not been present on examination three years previously. The patient stated that for some time she had had dyspnea on exertion but no other symptoms. The past history revealed no etiologic factor for these pulmonary findings other than Raynaud's disease. The patient had had no cardiac disease and no history of unusual or repeated pulmonary infections or exposure to dust. Repeated examinations of the sputum were negative for tubercle bacilli and other significant organisms. Roentgenograms of the lungs showed increased markings and diffuse mottling in the lower half of both lung fields, and displacement of heart and mediastinal contents to the left owing to atelectasis.

During the next year, the dyspnea, cyanosis and x-ray changes increased progressively, so that in the fall of that year the patient had constant respiratory distress, even at rest. An acute episode of severe respiratory embarrassment, pain in the right chest and marked cyanosis made hospitalization necessary. On admission the respirations were 70; the patient had slight fever, and there were many moist rales in both lungs from the angles of the scapulas down. The roentgenogram showed a pneumonic process at the right base. Oxygen therapy was started immediately and was continued until death, 46 days later. During the first few days the patient was reasonably comfortable while in the tent, but she developed extreme dyspnea and cyanosis when taken out for even a short time. Later, however, respiratory embarrassment and cyanosis increased progressively, even while the patient was in the oxygen tent. Death was apparently due to asphyxia. Permission for a post-mortem examination was not obtained.

Case 2. Mrs. B. F., a 39-year-old woman, entered the hospital complaining of intermittent attacks of 13 years' duration, during which the skin of the face, abdomen and hands became blue, especially when exposed to cold; she also experienced "pins-and-needles" sensations in her fingers. These attacks had increased in frequency during the several months prior to entry. For a few years the patient had noticed shortness of breath and palpitation on exertion, but had no other complaints.

Physical examination showed cyanosis of the face, tongue and hands, especially the finger tips. There was some atrophy of the skin over the distal phalanges, which appeared shortened. The fingers were stiff on attempted motion. Scattered under the skin of the hands and fingers were small irregular deposits of whitish material, which on chemical examination proved to be calcium salts. There was minimal narrowing of the retinal arteries. The blood pressure was 140/80. Examination of the heart, lungs and abdomen revealed no abnormalities. All laboratory determinations were within normal limits.

Roentgenologic examination of the chest showed exaggerated markings in the lower halves of both lung fields; the hilar regions were greatly increased in width and density, and the pulmonary conus appeared prominent. Roentgenograms of the hands showed partial destruction of the distal ends of some of the terminal phalanges, and small calcified bodies in the soft tissues that were consistent with the diagnosis of "calcinosis circumscripta." Roentgenograms of the feet, skull, femurs and genitourinary tract showed no deviations from the normal.

During the following months the symptoms progressed, and dyspnea and cyanosis were severe enough to require constant bedrest. During the few weeks prior to death, scattered moist rales developed at both bases, and slight edema of the ankles became evident, with no other signs of cardiac failure. Digitalization was without effect on the edema, rales or dyspnea. The patient died from respiratory failure 20 months after admission. Permission for a post-mortem examination was not obtained.*

Case 3. Mrs. E. S., a 30-year-old woman, had noticed for 3 years before admission to the hospital that her hands, fingers and feet felt numb and cold and turned blue on exposure to cold. The fingers, hands, elbows, knees and ankles were sore and stiff, and the skin was noticeably dry. For 8 months the patient had experienced easy fatigability, anorexia and lack of ambition. Examination revealed stiffness of the wrist joints and thickened fingers, fixed in flexion. The skin of the fingers, hands and forearms was cold, dry, shiny and brownish; the finger tips were reddish purple. Similar changes were present about the ankles and toes. The skin over the face, neck and anterior chest was indurated and dry. Pulsations were palpable in all the peripheral vessels. The blood pressure was 142/94. The heart and lungs were normal except for a vital capacity of 1600 cc.

Roentgenologic studies showed marked osteoporosis of the bones of the wrists and hands. The chest plate revealed moderate increase in width and density of the hilar regions, and slight mottling and diminished radiance at both bases.

Bilateral dorsal sympathectomy was performed, after which the patient developed a mild pneumonic process at the right base, which subsided in a few days. Following a bilateral lumbar sympathectomy, she developed a pulmonary embolus in the left lower lobe. The symptoms of weakness and dyspnea increased, however, and, in addition, cyanosis, cough and sibilant rales developed. The terminal stage of her illness began with chills, fever and consolidation at both lung bases. The patient also developed a pericardial friction rub and died in a few days. Permission for post-mortem examination was not obtained.

*We are indebted to Dr. Louis Silver for the history of Case 2 after the patient left the hospital, and to Dr. Samuel L. Gargill for his permission to report Case 3.

These 3 cases have similar histories. They all started with typical manifestations of Raynaud's disease that continued for several years. Then nutritional changes of the skin occurred, and scleroderma developed; some time later the patients began to complain of dyspnea on exertion. Coincidentally, roentgenologic examinations showed fibrosis in the bases of the lungs. In no case were there any factors that would explain the etiology of the pulmonary condition. None of them had evidences of cardiac disease; there was no history of repeated pulmonary infections, or of exposure to agents that might cause pulmonary fibrosis. The rapidity with which the fibrosis progressed and the severity and rapid development of the respiratory difficulty were very unusual, and were not typical of any of the usual types of progressive pulmonary diseases. All three patients died within three or four years after the onset of the dyspnea. In the last case, an intercurrent infection was the immediate cause of death.

Even in cases of extensive fibrosis of the lung due to silicosis, the progress is not so rapid, nor is the dyspnea so marked as that seen in these cases.

We were unable, unfortunately, to get post-mortem evidence that vascular changes in the lungs were responsible for the pulmonary fibrosis in the above cases. However, the rapid development of the changes in the lungs and the marked dyspnea and cyanosis existing together with Raynaud's disease and scleroderma suggest that the pulmonary fibrosis was due to vascular disease in the lungs, similar to that which takes place in the skin in Raynaud's disease.

Matsui[2] published complete post-mortem findings in 6 cases of diffuse scleroderma that were clinically similar to the cases reported above with respect to the hands and fingers. He found typical changes in the small vessels of all the organs, with secondary fibrosis of the parenchyma. Thus the changes in the small branches of the pulmonary artery, similar to those found in the digital arteries, were accompanied by extensive fibrosis of the lungs. The changes in the vessels were characterized by hypertrophy of the musculature of the media and fibrosis and thickening of the intima, with great narrowing of the lumen — changes characteristic of Raynaud's disease.

The situation in Raynaud's disease is thus analogous to that in thromboangiitis obliterans. Until recently the latter was regarded as a disease confined to the blood vessels of the extremities. In the last few years, however, after attention had been called to the fact that thromboangiitis obliterans may be a generalized vascular disease,[3] numerous reports of cases of involvement of the systemic arteries by the disease have appeared in the literature. A recent report from the Mayo Clinic[4] noted the occurrence of thromboangiitis obliterans in the coronary arteries, as well as a case of the disease in the pulmonary artery.

Raynaud's disease, as the foregoing histories suggest, should be regarded, not as being limited to the small arteries of the extremities, but as involving the small arteries of the lungs and possibly of other organs of the body. It is also possible that an occasional obscure case of pulmonary fibrosis is an exceptional example of Raynaud's disease without the typical manifestations in the digital arteries.

Summary

Three cases are reported, all starting with typical manifestations of Raynaud's disease. In the course of several years, scleroderma developed, with subsequent fibrosis of the lungs of unknown etiology. The suggestion is made that the pulmonary fibrosis was secondary to changes in the small vessels of the lungs as a part of Raynaud's disease, and that this disease is therefore not limited to the digital arteries or the arteries of the extremities, but may involve the arteries of the lungs and possibly those of other organs of the body.

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CLINICAL NOTES

MENINGOCOCCEMIA

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MENINGOCOCCEMIA is a relatively rare cause of intermittent fever accompanied by a rash and may present a real problem in diagnosis. This fact, as well as the demonstration that small doses of sulfanilamide are inadequate in preventing a recurrence of temperature and rash, makes it seem worth while to add one more case to the growing literature of this disease, which in the past has been considered a clinical rarity.

The disease was first described by Salomon[1] in 1902. In 1931, Binns and Fothergill[2] pointed out that the majority of cases had been reported in the foreign literature, only 19 being found in American journals. They reported a case in a child eight years old, who recovered after treatment with antimeningococcus serum. Since that time, each year four or more reports have appeared dealing with both the clinical and laboratory aspects of the disease.

Heinle[3] points out that there are two main types of meningococcal septicemia. The first is acute and fulminating and is invariably fatal; the second is chronic and lasts many months, with spontaneous recovery in many cases. The latter are fortunately in the majority. Lambie[4] reports a case that ran a self-limited course of three and a half weeks. He believes that meningitis should be regarded as only one metastatic lesion of meningococcal septicemia.

An excellent clinical description is given by Carbonell and Campbell,[5] who report 33 cases from the literature and 3 of their own. The symptoms and signs in the order of frequency are rash, intermittent fever, arthralgia, chills, headache and myalgia. They point out, as do most writers on the subject, the difficulty of growing the organism, even in enriched mediums.

The fever differs from malaria in that the daily peak does not occur at the same hour.[6] As a rule the patients do not appear toxic or acutely ill.[7] When first seen, the patient is thought to be suffering from ordinary grippe with general malaise, fever and myalgia. Shortly afterward, in from one to three days, a macular rash appears, usually on the extremities. Although it is pink at first, it may later be purplish or even hemorrhagic. There may be arthralgia.[8] The fever, rash and generalized symptoms disappear in twenty-four to forty-eight hours, only to recur at intervals of from one to four days. In the early stages, the disease is confused with measles, typhoid fever, Rocky Mountain spotted fever and malaria. Later the differentiation from gonococcemia may become difficult.

The chief laboratory problem is growing the organism from the blood stream. Serum-agglutination tests may be necessary.[7] The complement-fixation test may be positive,[6] a feature that is rarely mentioned in the literature.

The chief complication is meningitis, which usually occurs late. Endocarditis occurs in 10 per cent of the cases. Nephritis may develop, but is rare. Epididymitis is a not infrequent complication in men.[7] The arthralgia may go on to articular destruction and ankylosis.[8] The Waterhouse-Friderichsen syndrome, owing to acute bilateral suprarenal apoplexy, is often caused by meningococcal septicemia, but is usually seen only in infants and young children.[9]

Until the advent of chemotherapy, treatment was limited to the use of antimeningococcus serum[6] and fever therapy.[10] However, in the last few years, dramatic cures have been reported with sulfanilamide[11] and sulfapyridine; Dimson[12] favors the latter because of its quicker action and because a smaller dosage is necessary.

CASE REPORT

A 22-year-old unmarried woman while on Cape Cod on June 10, 1940, removed several ticks from her body, none of which had burrowed under the skin. Thirty-six hours later she had general malaise, chilliness and a temperature of 101°F., which lasted for 2 days. On June 16, 6 days later, the temperature again reached 101°F., and a maculopapular rash, which was hemorrhagic in spots, was present on the extremities. She was not toxic, and the physical examination was otherwise negative. On June 18, the rash was fading and the temperature was normal. On June 19, the temperature reached 102°F., general aching was present, and the patient complained of pain in the right knee. On June 20, the rash was more pronounced and had spread somewhat over the body. The macules could be blanched by pressure and were slightly raised and tender. The patient was referred to the Newton Hospital.

On June 20, the Widal test, Weil–Felix reaction, agglutination test for undulant fever and blood Hinton test were negative. The blood smear showed no plasmodia. A blood culture taken on June 22, when the temperature was 102°F., showed gram-negative intracellular diplococci that fermented glucose but would not grow in maltose. At this time, a history of leukorrhea, present for several years, was obtained. The patient admitted possible exposure to a gonococcal infection, and a tentative diagnosis of gonococcemia was made. She was started on 40 gr. of sulfanilamide a day. Vaginal smears on June 26 and 30 were negative for gram-negative intracellular diplococci. On June 26, there was a recurrence of fever, with chilliness and rash, and localized swelling and redness of the right 2nd and 3rd metacarpophalangeal

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joints. Complement-fixation tests for gonococcus, done on June 27 and 28, were positive. Organisms were again grown from the blood stream on June 25. These did not grow on maltose for 10 days, after which fermentation was present, thereby establishing the diagnosis of meningococcemia. She was discharged after 6 days of sulfanilamide therapy.

On July 8, there was a recurrence of temperature of 103°F., with rash, sore throat and aching of the back and knees. The patient was readmitted to the hospital by Dr. Lewis I. Pilcher, and was seen by Dr. Chester S. Keefer, who made a diagnosis of chronic meningococcal septicemia and advised intensive sulfanilamide therapy, with a blood level of not less than 10 mg. per 100 cc. This was carried out for 7 days. On July 18, a blood culture was negative, and on July 20 the patient was discharged.

When seen on August 21, the patient had had no recurrence and was clinically well.

This case was characterized by intermittent fever, arthralgia, a macular rash and very little evidence of toxicity. The diagnosis was delayed by the slow growth of the organism in maltose and the positive gonococcal complement-fixation test, coupled with a history suggestive of venereal disease. The question of Rocky Mountain spotted fever was raised because of the history of tick exposure. Haverhill fever was considered before blood cultures were positive. Sulfanilamide in daily doses of 40 gr. for six days was inadequate for complete cure, which was accomplished by seven days of intensive sulfanilamide treatment.

Summary

A case of meningococcemia that at first suggested gonococcemia because of the history and positive complement-fixation test is presented. Small doses of sulfanilamide were therapeutically ineffective, but the drug in doses sufficient to maintain a blood level of 10 mg. per 100 cc. for seven days effected a permanent cure.

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PNEUMOCOCCAL MENINGITIS SUCCESSFULLY TREATED WITH SULFATHIAZOLE AND ANTIPNEUMOCOCCUS SERUM*

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CINCINNATI

In 1939, Fosbinder and Walter[1] described two new derivatives of sulfanilamide that gave promise of clinical usefulness. Since that time, sulfathiazole has been reported as being of value in the treatment of pneumococcal and staphylococcal infections, and this has been confirmed in our own experience. Recently, we have had an opportunity to administer sulfathiazole to a patient with pneumococcal meningitis with very encouraging results. Because a review of the literature fails to disclose a similar instance of its use, we are reporting the case.

Case Report

A. L., a 50-year-old man, was admitted to the Ophthalmic Service on June 28, 1940, complaining of inability to see out of the left eye. He had had four abscessed teeth removed on May 5, 1940. Following the extraction, he felt quite well until he was stricken with pain in the left eye 3 days prior to admission. Examination at that time revealed an exquisitely tender eye, with pus in the anterior chamber. A diagnosis of acute purulent endophthalmitis, probably metastatic, was made. Expectant treatment failed to bring relief, and an enucleation was performed on June 30. No evidence of orbital infection was noted at operation. The postoperative course was satisfactory and without fever until the evening of July 6, when the patient complained of pain in the right side of the neck; the temperature at this time went to 103°F. by rectum. The sensorium became clouded, and the patient soon became very unco-operative, although not comatose.

Lumbar puncture disclosed a clear fluid under slightly increased pressure; it contained 600 leukocytes per cubic millimeter, of which 60 per cent were granulocytes. Culture of the fluid showed a luxuriant growth of Type 3 pneumococcus. Blood culture on the same day showed no growth.

Oral administration of sulfathiazole was begun at once; the initial dose was 4 gm., and subsequent doses of 2 gm. were given every 4 hours. Twelve hours later the patient was given 240,000 units of Type 3 antipneumococcus serum intravenously. The improvement was prompt and striking. Within 72 hours of the onset, the spinal fluid was sterile and the temperature reached normal. Chemotherapy was continued for 6 days, a total of 67 gm. of sulfathiazole having been administered.

A summary of the laboratory findings is given in Table 1. Convalescence was uneventful except for an attack of lum-

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This study was aided by a grant made in honor of Craig Yeiser.

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bar pain on the 6th and 7th days of chemotherapy; this, in turn, was followed by a very minor degree of hematuria. Blood chemical determinations at that time showed not only an unusually high free concentration of sulfathiazole, but also a very high level of the conjugated drug. Following the discontinuance of chemotherapy, the pain promptly subsided and the hematuria gradually disappeared.

The pathogenesis of the meningitis in this case is very obscure. Cultures of the pharynx and the teeth sockets yielded no pneumococci. Roentgenograms of the sinuses and air cells of the skull disclosed no focus of infection. Unfortunately, fluid from the hypopyon was not cultured; a culture from the left eye socket showed no pneumococci. The patient did not have pneumonia. Inasmuch as pneumococci are frequent causative agents of hypopyon, it is not unreasonable to suspect that the meningitis represented a late metastatic lesion from the endophthalmitis.

The employment of two specific agents in the treatment makes it impossible to evaluate either remedy. The patient was improving on sulfonamide therapy alone before serum was administered; combined treatment was instituted because of our uniformly discouraging results in the treatment of pneumococcal meningitis, and because of certain evidence that combined therapy may be indicated generally in Type 3 infections. It may be possible, however, that sulfathiazole diffused through the blood-brain barrier to create a concentration in the spinal fluid that was equal to those in the blood stream that are frequently associated with bacteriostasis. Moreover, no serum or complement was introduced intrathecally.

TABLE 1. *Summary of the Laboratory Findings.*

DATE	SULFATHIAZOLE DOSAGE	WHITE-CELL COUNTS		CULTURES		SULFATHIAZOLE LEVELS*	
		BLOOD	SPINAL FLUID	BLOOD	SPINAL FLUID	BLOOD	SPINAL FLUID
	gm.	*per cu. mm.*	*per cu. mm.*			*mg./100 cc.*	*mg./100 cc.*
7-6			600	Negative	Pneumococcus (Type 3)		
7-7	11	14650	1150		Pneumococcus (Type 3)		Trace
7-8	12		746		Pneumococcus (Type 3)	4.2	1.5
7-9	12	7950	193		Negative	7.2	1.4
7-10	12		99		Negative	8.4	2.0
7-11	12	7550					
7-12	8		59			13.7	
7-13	2	14600			Negative	14.0	3.5
7-14		12900				12.8 (free) 9.4 (conjugated)	
7-15		13250				5.8 (free) 7.6 (conjugated)	
7-16		7300					
7-17			5	Negative		0.8	
7-22							
7-27		7100	5				

*Chemical determinations were made according to the method of Bratton and Marshall,[2] using a sulfathiazole standard.

SUMMARY

A patient with Type 3 pneumococcal meningitis recovered promptly after treatment with sulfathiazole and antipneumococcus serum.

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MEDICAL PROGRESS

ALLERGY: WITH SPECIAL REFERENCE TO DRUG ALLERGY*

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THE current literature dealing with allergy contains an increasing number of reports of queer reactions to queer substances. There are various reasons for this. First, the principles of allergy are being recognized more and more, and the profession and the public are becoming "allergy conscious." Secondly, with the help of allergic principles, many lesions particularly those of the skin, that were formerly passed off as being of minor importance can now be recognized as having a real cause and are reported as such. And thirdly, modern progress, particularly in chemistry, has resulted in the development of a host of new substances encountered in industry, as well as in new forms of medical treatment. More of these new substances are appearing from time to time, and reports of reactions continue to be presented. It is therefore considered worth while to review the present knowledge of the subject.

The fundamental principles are not difficult to understand. The state of hypersensitiveness is acquired by certain people but not by everyone; and this fact raises the question whether the capacity to develop sensitiveness is in itself an unusual and distinct function or whether it is merely an exaggeration of a normal response. The arguments for and against each of these conceptions need not be reviewed here. The fact is that when the person who has the capacity to develop sensitiveness comes into repeated contact with a new foreign substance, he is likely to develop a hypersensitiveness to it. The nature of the foreign substance seems to be relatively unimportant, for as will be seen presently, sensitiveness may be developed to substances of such simple chemical structure as iodine, arsenic and aspirin, or to those of such complexity as egg-white and horse serum at the other end of the scale. The list contains substances of all chemical varieties between the two extremes.

Sensitiveness may arise in various ways and may take on various forms, perhaps in accordance with the mode of exposure. In general, there are two major groups.

The first is *local tissue sensitiveness*, which may develop without evidence of changes in the body as a whole. It is limited to one kind of tissue, usually the skin, as shown by the fact that in poison-ivy dermatitis the patient can eat the leaves without symptoms, since his mucous membranes are not sensitive. Under the title of "contact dermatitis" a multitude of reports deal with variations in the application of the principles. In other cases, the sensitiveness may be of the mucous membranes rather than of the skin, and one may have lesions of the eye, the mouth (canker sores), the nose (hay fever) or the vagina, all without evidence of sensitiveness in other tissues, as might be shown by positive skin tests or by the presence of skin-sensitizing antibodies in the blood. Whether asthma can be due to a sensitivity localized in the bronchial mucosa is an interesting possibility. In this group of local tissue sensitiveness, skin reactions made by the scratch method are quite negative. Contact dermatitis has been known a long time. The patch test, which reproduces the lesion and confirms the diagnosis, was described by Jadassohn[1] in 1895, which was seven years before Portier and Richet[2] reported on "anaphylaxis," and eleven years before Von Pirquet[3] discussed "allergy." As Sulzberger[4] remarks, this early work is not often recalled.

The second major group is *general sensitiveness*, that is, a reaction of the whole body. In hay fever, asthma and certain types of dermatitis ("eczema"), the exciting factor, which occurs in dust or foods or drugs, is absorbed into the blood and thus reaches the shock organs in the nose, the bronchi or the skin. The sensitiveness can be transferred locally to normal persons by injecting the skin-sensitizing antibodies of the patient's serum. Skin tests are usually positive.

The relation between hay fever, asthma and flexural eczema of the typical allergic, or more properly called "atopic," varieties, and the less well-defined drug rashes, urticarias, general systemic reactions and blood reactions is not always clear, but at least one can say that they occur in only a small number of persons who are specifically sensitized and that the nature of the symptoms suggests that the process is general and not local. The distinction between reactions that are allergic and those that are toxic depends on whether they occur in only a few patients or quite regularly in all persons exposed to the drug. In other words, the

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question is, Does the reaction depend on some change in the particular patient, or is the drug poisonous for all? In a few cases of drug allergy, positive skin tests and skin-sensitizing antibodies have been observed. Whenever the skin is involved, the patch method of testing usually gives positive results; but when the skin is not involved, neither by the scratch nor by the patch

TABLE 1. *Drug Allergy.*

LOCAL TISSUE SENSITIVENESS
Contact dermatitis (skin)
Mucous-membrane sensitiveness
Eye (conjunctivitis)
Nose (hay fever)
Mouth (canker sores)
Bronchi (asthma)
Vagina (vaginitis)
Fixed eruptions
GENERAL SENSITIVENESS
Atopy (hay fever (?), asthma, atopic eczema)
Systemic reactions (including asthma)
Dermatitis medicamentosa
Urticaria
Blood dyscrasias (agranulocytosis, purpura, aplastic anemia)
Miscellaneous (migraine, joint pains, dysmenorrhea and so forth)

method can the sensitiveness be demonstrated. The relation between the two major groups and their subdivisions is shown in Table 1, and the various points are considered in the following sections.

LOCAL TISSUE SENSITIVENESS

Contact dermatitis is common and may depend on any one of an almost indefinite number of drugs. Sulzberger[4] gives a list of eight hundred different substances that he has used for patch tests in persons suspected of being sensitive to one or the other. The list is similar to that published in 1939 by Rostenberg and Sulzberger.[5] On the last page of Sulzberger's paper, one notes, among other items, water colors, Whitfield's ointment, window sprays, oil of wintergreen, witch hazel, xylol, yellow oxide (a dye), zinc sulfate and Zonite, in other words, dyes, medicaments, household chemicals, cosmetics, industrial chemicals and patent medicines — the whole range.

Recent case reports are numerous. Downing's[6] patient was a window glazier who became sensitive to the orthodichlorobenzene used as a wood preservative. A drop of the solution applied to the arm produced intense erythema and edema in two minutes. In Walter's[7] patient, hexylresorcinol was applied externally each day for five months. Two years later, the drug was applied again and a severe local dermatitis resulted in vesicular, bullous lesions. Goodman[8] observed positive patch tests in a patient with severe contact dermatitis who was poisoned by various local anesthetics. He found, however, that only those anesthetics with a para-aminobenzoyl base caused reactions. No response followed when the amino group was in the meta or ortho position, and other cases have shown that the development of sensitiveness depends not only on the chemical constituents of the substances involved but also on the way in which they are arranged in the compound. Schwartz and Russell[9] describe an extensive dermatitis in a patient who was found sensitive to the resin used for lining tin cans. So-called "can poisoning" is not uncommon. On the other hand, Henry[10] found that his patient was sensitive to the celery oil in the contents of a can.

Mucous-membrane sensitiveness occasionally occurs, and cases must be looked for. In 1935, Parlato's[11] patient was a nun who developed corneal ulcers after exposure to sachets used in the church vestments. She gave a markedly positive skin test to orris powder so that her trouble was of general, rather than local origin. Pfeiffer's[12] patient was sensitive to Pontocaine, so that 2 drops of the 0.5 per cent solution in the eye resulted in the development of massive edema of the eyelids, face and parotid regions that came on in a few hours. Patch tests were positive. Somewhat similar is the case reported by Theodore,[13] who found his patient sensitive to Larocaine. Parkhurst and Lukens's[14] patient was sensitive to Butyn, and when a 2 per cent solution was dropped in her eye, both eyes became markedly swollen. Patch tests with Butyn and also with a solution of zinc sulfate were positive. In each of these cases, the sensitiveness of the eye was very marked, but one could hardly say that it was limited to this particular mucous membrane.

That vernal conjunctivitis is an atopic illness and not a local process is the conclusion of Lehrfeld and Miller,[15] who studied 120 cases. Many positive skin tests with foods and drugs were found, and the eosinophils were high in both the blood and ocular smears.

In the vagina, local sensitiveness has been recognized. Kesten[16] treated a woman for Trichomonas vaginitis, using a powder containing arsenic. In a few minutes, burning and itching developed and became intense, and were followed promptly by a red rash. Whereas the lesion was marked in the mucous membrane, it spread to the skin of the inner aspects of the thighs as well.

A local sensitiveness of the nasal mucosa is a possibility that might account for the fact that certain patients have hay fever but give no positive skin tests to pollens. Occasionally, eye tests made by dropping crude pollen into the conjunctival sac are positive, or further study shows that the skin tests, which were negative in the first years, become positive in later years, suggesting that the disturbance is quite local at first but later spreads

to involve the body as a whole. It may be that certain cases with asthma can be shown to have a similar mechanism dependent on a localized, perhaps "fixed," sensitiveness of the bronchial mucous membrane.

The so-called "fixed drug eruption" was, according to Sulzberger,[4] described first by Brocq in 1885. Sulzberger recalls that Brocq observed a patient who developed sharply circumscribed, elevated, discolored eruptions whenever a dose of Antipyrine was taken by mouth; these lesions always recurred in the same spots. Here, then, is evidence not only that the skin as a whole may be sensitized, but also that some areas of the skin may be more sensitive than others. Sulzberger reports that in some patients, certain fixed areas will react to one drug whereas others will react to another drug. His patient had a lesion on the hand that flared up regularly when she took a dose of a barbiturate by mouth, and she also had a fixed area on her thigh, which reacted when she took phenolphthalein. The hand did not react to the cathartic, nor did the thigh react to the sedative. Sensitiveness was not only localized—it was highly specific. Meredith[17] observed a thirty-nine-year-old woman who had two round inflamed areas on the neck and one on the thigh. In a series of experiments, it could be shown that any barbiturate, such as Allonal, Sedormid, Dial or Sodium Amytal,—the last being the worst,—could cause a flare-up in these particular areas. The literature has been reviewed by Wise and Sulzberger,[18] and more recently by Abramowitz and Noun.[19]

General Sensitiveness

General sensitiveness is somewhat easier to understand, since the vast number of patients with so-called *"atopy,"* that is, hay fever, asthma and atopic eczema, provide typical illustrations. The capacity to develop this type of sensitivity is inherited: skin tests are positive, and skin-sensitizing antibodies can be demonstrated in the blood. It is important to keep the group in mind as the more general effects of drug allergy are considered briefly from here on.

Systemic reactions from drugs are not unknown. In 1933, Short and Bauer[20] reviewed the literature on cinchophen hypersensitiveness. They found 41 cases and added 4 of their own. All were made sick by the drug, and 3 patients developed urticaria. In 1937, Boros[21] described a patient who developed jaundice and later ascites after taking cinchophen. In 1938, Sugg[22] collected 32 cases of cinchophen poisoning, 22 of which had evidence of liver damage; 10 of these patients died; 10 others had extensive skin lesions, and 2 died. The drug was toxic.

Avertin caused death in 7 cases reported by Beecher,[23] who discusses the differences between allergic reactions and toxic effects, emphasizing that severe reactions occur only in a few people and thus point to a change in make-up. More recently, Dolan[24] and Crane[25] have described the occurrence of sudden death following the intravenous administration of an iodine-containing dye, called Diodrast, used in urography. In hundreds of other cases, it has caused no trouble.

Acute asthma can be caused by drugs. The asthmatic patients sensitive to acetylsalicylic acid (Aspirin) form almost a special group, because they are always difficult to deal with. Objective tests with the drug are unsatisfactory: the skin test is negative. Several reports of such cases were summarized in 1937 by Prickman and Buchstein.[26] In the same group, but less common, are other cases. Martinaud[27] observed a fatal attack of asthma that came on when the nasal mucosa was washed with a solution of Butyn. An injection of quinidine caused angioneurotic edema of the lips and larynx, and the next dose caused urticaria, shock and death, in a patient reported by Breu and Zollner,[28] the only case of quinidine poisoning in the literature. Another report is that of the McCastors,[29] who in five days after the first dose injected sodium morrhuate into the varicose veins of a thirty-year-old man. Suddenly he turned pale, then became cyanotic and collapsed, but with artificial respiration, epinephrine and Coramine he revived slowly. In another case, a similar though less violent reaction followed injection of sodium morrhuate into a hydrocele. The authors emphasize, however, that these were the only reactions in a series of twenty-five hundred injections. Two industrial chemicals are reported as a cause of asthma. Card's[30] patient was sensitive to the chromium used in a plating factory, and Kern's[31] patient was sensitive to phthalic anhydrate, a dye made from naphthalene.

Dermatitis medicamentosa is an old term that appears in many textbooks, and under it the generalized rashes due to bromides, iodides and arsenic salts are often described. In the literature up to 1937 Seymour[32] found reports of 14 cases in which the local application of iodine had caused severe generalized eruptions; 7 of these were fatal, and he added another case. In 1937, Beijerinck[33] added a sixteenth, and also fatal, case of so-called "ioderma" with extensive generalized dermatitis caused by the injection of 1 gm. of potassium iodide daily for fourteen days.

Fanburg[34] has described a patient with exfolia-

tive dermatitis due to naphthalene on clothes stored in a moth-proof closet.

In 1932, Bullen, Francis and Parker[35] reported 2 cases in which the ingestion of ephedrine caused the development of a generalized dermatitis followed by desquamation, and the next year Scheer and Keil[36] reported on scarlatiniform eruptions after codeine. Gelfand[37] observed a woman who had marked generalized dermatitis from the application of a hair tonic and dandruff remover, and Settle[38] described the case of a young man whose extensive skin lesions were due to quinine. Baker and Brunsting[39] observed the sulfocyanates as a cause of dermatitis, and Brandt[40] discovered that the recurrent eczema in a forty-five-year-old woman came and went as her digitalis was prescribed or omitted.

The reactions to arsphenamine are of more practical importance. They occur oftener during the first course of treatment, and thus may depend more on the toxicity of the drug than on the allergy of the patient. Dermatitis is a contraindication to further treatment — at least with the particular preparation that caused it. Schoch, Alexander and Long[41] have recently collected a series of cases and have shown that in most of them, treatment could be tolerated without further trouble. They suggest that the sensitiveness is directed not to the arsenic itself but to the particular chemical complex of which it is but a part. The Herxheimer reaction is said to be due to the flare-up of the syphilitic lesion, like the so-called "provocative Wassermann reactions" in vogue some years ago. It may also be a form of local allergy. Nitritoid crises are immediate reactions with flushing of the skin, palpitation, collapse and sometimes asthma from edema of the bronchial mucosa, which come on suddenly, immediately after or often during the actual injection of arsenicals. Since these reactions occur in only a few patients, one may assume that allergy plays a part. They provide another illustration of the acute systemic responses described above.

Comparative studies of similar phenomena are as useful in allergy as in chemistry. Professor Sanger, who used to lecture in elementary chemistry at Harvard College, demonstrated that the physical and chemical properties of the elements varied in a rather orderly fashion in accordance with their atomic weights, and he predicted correctly that several blanks in his large periodic table would be filled in. And so it is with drug allergy. The sulfanilamide drugs have complex formulas: they produce severe general reactions occasionally, and now that they are being used more and more for purely local treatment, local contact dermatitis can be almost expected; so far, however, I have not seen them. Toxic reactions, on the other hand, have been reported frequently, especially after later doses, when the drug had been repeated in a new and separate course of treatment, and deaths have occurred. Long and Bliss[42] reviewed the literature up to 1939. They did not mention local reactions, but two reports (Tedder,[43] Hallam[44]) lay stress on photosensitivity, which gave rise to extensive skin lesions in patients who had taken sulfanilimide or sulfapyridine and then were exposed to the sun or to an ultraviolet lamp. In these cases, the reaction was of a special type and consequently more toxic than allergic, even if observed in only a few of many patients.

Urticaria may be due to drug allergy. Indeed, urticaria and erythema multiforme are often part of the severe systemic reactions described above. Urticaria may also precede and be a part of generalized skin reactions. Reports of pure urticaria from drugs alone are not common. One difficulty is that whereas salicylates, barbiturates, morphine, iodine and phenolphthalein have been suspected as the cause of urticaria, — since rashes appeared when the drugs were given and cleared when they were withdrawn, — other factors are always hard to control. There is no doubt, however, that drugs of any sort are quite capable of causing hives.

Blood dyscrasias comprise another chain of symptoms that depend on a generalized sensitiveness of the body. Primary granulocytopenia (agranulocytosis) was first described in 1922 by Schultz,[45] but was first recognized as being due to drug poisoning by Squier and Madison[46] in 1933. In 1935, Hunter[47] reviewed the literature completely and pointed out that in most cases there was a story of previous use of the drug, and an interval before the second use, which caused the severe attack. The triad of first dose, interval and second dose may be compared with the anaphylactic experiment. In 1936, Dameshek and Colmes[48] were able to combine amidopyrine with serum to make a drug-protein linkage and thus to substantiate the role of allergy as the background for agranulocytosis. Between 1934 and 1938, cases sensitive to amidopyrine were reported with some frequency. Since then, the reports have been fewer, evidently because the dangers have been recognized and precautions in the way of careful following of the blood picture have been instituted.

Purpura from drugs is not uncommon, and the literature has been reviewed by Falconer and Schumacher[49] and by McGovern and Wright.[50] Sedormid (allylisopropyl-acetylcarbamide) seems to be a common cause, for it is reported several times

in recent literature. Purpura has followed the use of gold and arsenic compounds, as described by Hudson,[51] and was caused by quinine in the case reported by Beiglböck.[52]

Aplastic anemia may likewise be due to an allergic reaction caused by drugs. It has been found to follow the use of neoarsphenamine. Kadin[53] reviews the literature and adds 3 cases of his own.

It is very hard to determine why in certain people allergy causes a lesion of the bone marrow affecting the white cells, whereas in others it results in a disturbance of the blood platelets. One can speculate on the variations in the sensitivity of certain parts of the blood-forming mechanism and compare them with the different forms of contact dermatitis, — a sensitiveness of the skin in general, and the fixed drug eruption, in which only a portion of the skin is affected, — but there is no real knowledge of the subject.

Certain *miscellaneous diseases* deserve mention. Headache (migraine), joint pains and dysmenorrhea have been described as due to specific foods, but there is no report that incriminates drugs as a definite proved cause of these common symptoms. The possibility is included here merely as a suggestion and with the expectation that this blank also will be filled in. Sensitivity to hormones — insulin and liver and pituitary extract — occurs in occasional cases and rests quite firmly on a basis of allergy. Guinea pigs have been sensitized to crystalline insulin by Berstein and his associates.[54] Certain patients may be sensitive to the insulin alone, just as other patients appear to be sensitive to the animal from which the insulin was obtained and are relieved of trouble when the type of insulin is changed as from beef to hog. Similarly, in pituitary extracts, Simon and Ryder[55] found that sensitiveness depended on an organ-specific rather than a species-specific quality of the material.

Discussion

The principal object of this brief review has been to call attention to the subject of drug allergy. It is not a very common disease, but it occurs often enough to be considered whenever a queer reaction occurs and results in a clinical picture that does not quite fit a recognized disease. One should think of the possibility that such a reaction depends on a hypersensitiveness to a queer substance: perhaps a drug, or perhaps some special chemical substance associated with home or occupation. Also, it is evident that drugs may be the principal cause of such definite conditions as asthma, urticaria, purpura and agranulocytosis.

Another object of this review has been to call attention to the multiplicity and the variety of reactions that drugs can produce, and then to arrange them in some sort of order so as to show the relation of one to the other and the relation between them and the better known clinical manifestations of allergy, like hay fever and asthma. It is emphasized that a hypersensitiveness to drugs may take on different forms and may result in a variety of different syndromes.

Finally, it appears that a study of the reactions to drugs is of considerable interest in its bearing on the reactions to other substances, especially the proteins and the pollens. The study of contact dermatitis is of particular importance because it suggests that sensitiveness may be localized to certain tissues or may at least be much more marked in one tissue than in another. This idea is similar to Coca's conception of a "shock organ," but the present emphasis is on the mechanism of the reaction, which is localized and results from direct local contact and consequently differs from the mechanism of other reactions, which, in turn, are more generalized and develop from contact with the specific substances through the blood stream.

This conception of local tissue hypersensitiveness needs much more study. The cases of contact dermatitis support the idea quite well, but when one tries to apply the same conception to the study of the mucous membrane, good support is hard to find. On the other hand, it is true that among hay-fever patients, there are some whose symptoms are typical, whose tests of the skin are quite negative, but who do react when pollen in crude dry form is dropped into the eye. Here is real evidence of a purely local process. The understanding of the problem of contact dermatitis becomes easier when that of hay fever is understood, and vice versa. Incidentally, is not ragweed hay fever in the nose of one patient and ragweed dermatitis of the face and wrists of another evidence of the varying predisposition of different local tissues? In this reaction, however, the chemical difference between the oleo resin, which can penetrate the skin, and the protein, which is soluble in the nasal secretion, may be significant. One's outlook must always be as broad as possible, so that one set of circumstances can be compared with the other, with profit to both.

Meanwhile, nothing has been said concerning the treatment of drug allergy. It should almost go without saying that treatment is synonymous with the diagnosis, which depends on two factors: first, thinking of the possibility, and secondly, studying the history. Just as in the study of hay fever and asthma, the dates and the circum-

stances of the attack give the clues by which the good detective can find the answer. Skin tests, especially by the patch method, are useful, but are positive only when the skin itself is involved. Drug allergy gives further evidence that clinical sensitiveness can exist even when the skin tests are negative.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 27161

PRESENTATION OF CASE

First Admission. A fifty-three-year-old housewife entered the hospital complaining of dysmenorrhea.

The patient had been well until seven years previously, when her normal periods became irregular. Each year for the next three she suffered four attacks of transitory but severe lower abdominal pain, which occurred on the third day of what appeared to be a normal period. The pain was relieved in a short time by the onset of rather pronounced vaginal bleeding, which lasted several days. Four years before admission the menstrual periods became more regular, and the patient noticed hot flashes of decreasing severity. Two years later another attack of abdominal pain occurred, which was relieved by the onset of bleeding and the passage of "tissue"; no further attacks of this nature had appeared, but menstruation became more irregular and scant and generalized weakness came to the fore. A year and a half before admission the patient had a normal menstrual period. Six months prior to entry marked the onset of a brownish, odorless vaginal discharge, with occasional bright-red streaking, accompanied by a dragging sensation in the pelvis, and low backache; these symptoms persisted and were present at the time of admission. In addition the patient noticed that her hair was becoming dry and sparse, and that frequent headaches occurred that were more noticeable in the morning. Three months before admission she suffered an attack of upper abdominal pain, which lasted four days and was accompanied by nausea, loose yellow stools and "darkening" of the skin. Her physician could not detect jaundice, and there was no visible change in the urine. A bland fat-free diet was instituted, and the attack was not repeated; the patient had never liked fatty food and was troubled by "gas on the stomach." Furthermore, she stated that she had shaved once a day for "years," had lost weight in the past few months, and had noted stinging pain in the fingers and toes for an undisclosed period.

The patient had five children who were well; she had had three miscarriages. Seventeen years before entry, a uterine suspension had been performed at another hospital.

On examination the patient was well developed, somewhat obese, and in no acute distress. The hair of the scalp was dry and receding, and there was facial hirsutism; the skin appeared atrophic. The heart, lungs and abdomen were negative apart from a mid-line surgical scar between the umbilicus and symphysis pubis; the blood pressure was 220 systolic, 100 diastolic. Pelvic examination revealed an enlarged clitoris with a relaxed perineum. The cervix was freely movable, and the fundus was normal in shape, but slightly enlarged. The vaults and adnexa were clear. Examination of the nervous system and eyes was negative except for a mild vascular sclerosis of the retinal vessels.

The temperature, pulse and respirations were normal.

Examination of the urine was negative. The blood showed a red-cell count of 4,940,000 with a hemoglobin of 94 per cent, and a white-cell count of 8400. The nonprotein nitrogen of the blood serum was 19 mg. per 100 cc. A sugar-tolerance test using 50 gm. of glucose showed a fasting blood sugar of 90 mg. per 100 cc., in half an hour 143 mg., in one and a half hours 204 mg. and in three hours 171 mg. The insulin-glucose-tolerance test showed slight insulin resistance. A blood Hinton reaction was negative, and a phenolsulfonephthalein test was normal. The cervical culture was negative for beta-hemolytic streptococci. Assays for 17-ketosteroids on two occasions gave values of 3.9 and 5.5 mg. in twenty-four-hour urine specimens.

X-ray studies of the chest were negative. A Graham test and intravenous pyelogram showed normal gall bladder and kidneys. Air injections revealed no enlargement of the adrenal glands.

An electrocardiographic recording showed a normal rhythm with a rate of 80 and a PR interval of 0.15 second. There was slight right-axis deviation and slight inversion of T_3.

On the third hospital day, a pelvic examination under ether and a dilatation and curettage were performed. The cervix had apparently been amputated at a previous operation, and it was found that firm adhesions had formed across its mouth, which required division before the os could be found. The fundus was of average size, and 10 cm. in depth; the vaults were clear, and no masses were palpable in the flanks. Curettage yielded three fragments of endometrial tissue resembling endometrial polyps; elsewhere the interior of the uterus was smooth. Pathological examination of these fragments revealed chronically inflamed cervical

polyps; no endometrial tissue was identified. The patient was discharged three weeks after admission.

Second Admission (six months later). The patient remained well until three months after discharge, when slight vaginal bleeding reappeared. It was bright red, sometimes had a slightly unpleasant odor, and occurred at intervals of two or three weeks, lasting two to seven days. At this same time she suffered from transient attacks of nonradiating lower abdominal aching and soreness that coincided with the bleeding or was independent of it. One month before admission she visited the Out Patient Department, and the examiner believed a mass to be present in the left vaginal vault. At the time of admission, the patient stated that her head felt full and thick and that her memory was poor.

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Physical examination was as before, with the following additional and contributory findings. The skin was oily, with a generalized mild acne. The blood pressure was 180 systolic, 115 diastolic. There were tenderness and slight spasm in both lower quadrants of the abdomen. The vagina contained blood, but the degree of tenderness in both vaults prevented an adequate examination.

On the third hospital day an operation was performed.

Differential Diagnosis

Dr. Maurice Fremont-Smith: It may be well to start off by pointing out that this woman was perfectly normal up to the time of the menopause. She had had normal periods and had had five children. That is satisfactory evidence that she was, from the endocrinologic point of view, normal. She began having irregular periods at the age of forty-six, which is a normal time for the onset of the menopause. She had attacks of lower abdominal pain occurring on the third day of bleeding and relieved after the bleeding got under way. The chief complaint simulates dysmenorrhea. Of course, unless one uses the term "dysmenorrhea" to include all painful bleeding, this is not dysmenorrhea. Dysmenorrhea characteristically occurs early in life, rarely when a person has had a number of children. In fact, to have children is one of the best treatments of dysmenorrhea. It does not start at this age. This was painful bleeding, and should be put in the group with ectopic pregnancy, miscarriage, endometriosis and pelvic inflammatory disease, all of which produce pain with bleeding but are not what we term "dysmenorrhea." The cause of this painful bleeding is, I think, adequately explained by the later findings. The cervix having been amputated, scar tissue had grown over the end, and when she menstruated, she bled into the uterus; the uterus tried to empty itself and could not; the patient had the same sort of pain that occurs with threatened miscarriage. When blood passed, the pain was relieved.

Four years before admission the periods became more irregular, and the patient had hot flashes, which, again, are perfectly normal menopausal symptoms. The hot flashes show that the pituitary gland was working, putting out follicular stimulating hormone, and an assay would have shown that follicle-stimulating hormone was present. The hot flashes grew less frequent. I think that was probably normal, as she adjusted herself to the increased follicle-stimulating hormone.

Two years before admission the patient complained of generalized weakness. That may be an important symptom to remember. At fifty-one she had a so-called "normal period." In other words, she had bleeding without pain and may have had what might again be normal — a period of anovulatory bleeding coming once after the beginning of the menopause. Six months later she had discharge, with bright-red streaking. Discharge after the menopause naturally brings up the question of carcinoma of the uterus. I think we can quickly dispose of that, however, because a thorough ether examination and curettage showed an atrophic endometrium, a few cervical polyps but certainly no cancer of the fundus, which would be the type of cancer expected at this age. The patient also had headaches, which we must remember, and she had sparse hair, to which I am unable to attach any significance. She had this queer attack of upper abdominal pain and yellow stools, with no apparent jaundice, and later she showed a diabetic sugar curve. She might have had an attack of mild, acute pancreatitis. She apparently did not have what one would first think of, — gallstones, — because she had a negative cholecystogram. Of course one can have gallstones in the presence of a negative cholecystogram, but she had no jaundice and no further attacks, and we either have to leave it unexplained or consider that she had an attack of pancreatitis.

The patient had shaved once a day for years. It would be helpful to know whether the hirsutism came on at a specific time in adult life or whether it fell into the very much larger group of hirsutism that has no endocrinologic basis. In 90 per cent of cases, hirsutism comes on at about the age of puberty and is due to disease of the hair follicles, which respond excessively to the normal steroids of the body. The end organ is at fault, not the endocrine glands. On the other hand, hirsutism can be evidence of a masculinizing process, but I think the fact that she shaved for years prob-

ably throws it into the larger group of congenital hirsutism.

The stinging pain in the toes and fingers, I cannot comment on.

As to the physical examination, there are some very important points. The patient was obese; the hair of the skull was receding; she had facial hirsutism. She had an atrophic skin, a high blood pressure and evidence by electrocardiogram of coronary arteriosclerosis. She had an enlarged clitoris. There was nothing abnormal in the vaults. These symptoms suggest Cushing's syndrome. We should like to know whether she had any osteoporosis. We have no x-ray films of the bones, but in Cushing's syndrome obesity is present, in addition to striae,—which are not mentioned here,—hypertension, arteriosclerosis, and a diabetic type of sugar curve.

Let us for a moment talk about the sugar curve. There was a glucose-tolerance curve of the diabetic type, and then we are told that there was slight insulin resistance. In ordinary diabetes we have, of course, a diabetic curve. If insulin is given, the curve is lowered. If one gives an insulin-glucose-tolerance test in which the insulin and glucose are balanced, one gets a rather flat curve. The sugar does not go up very high. In such a case the insulin is effective. In diabetes the reason that the sugar is high is that there is lack of insulin. We have been taught that insulin increases the tissue utilization of sugar. Soskin* says that in diabetes the tissue use of sugar is perfectly normal and that insulin acts by slowing down the production of sugar from the liver (which is constantly putting out sugar into the blood), but wherever insulin acts in diabetes, the insulin is effective on the blood sugar. There are two other conditions, however, in which insulin is not effective. With an overactivity of the eosinophilic cells of the pituitary gland, there is an overproduction of the hormone that inhibits insulin—the glycotropic hormone of the pituitary. If a glucose-tolerance test is performed and insulin is given at the same time, the insulin is inhibited by the pituitary hormone and is not active. Therefore, the curve is much as it was originally—very little influenced by the insulin. The curve approaches the diabetic curve, and the insulin is not effective. Another condition in which insulin does not change the diabetic curve is hyperactivity of the adrenocortical cells, which is thought to be the physiologic explanation of Cushing's disease. In such cases the adrenocortical cells produce a hormone that breaks down protein in the body into sugar very rapidly. There is thus an overproduction of sugar, and the insulin that is added—there being enough insulin in the body anyway—does not affect the glucose-tolerance curve.

Going back to Cushing's disease for a moment, Cushing's disease is due to an overactivity of the cortical cells of the adrenal glands. It was originally described as a basophilic tumor of the pituitary gland, the latter stimulating the adrenal glands to the production of the adrenotropic hormone, which, as previously mentioned, breaks down protein into sugar. On the other hand, some cases of Cushing's disease show no tumor of the pituitary gland. Some of them simply show hyperplasia of the adrenal glands, and in others Cushing's syndrome may occur with cancer of the adrenal glands. In all these cases, there are questionable compensatory changes in the pituitary gland. Apparently Cushing's syndrome can occur either as a primary condition in the adrenal glands, primary overactivity or as a secondary overactivity caused by a basophilic tumor of the pituitary gland. As I have said, many of these physical signs are consistent with Cushing's disease, as is the glucose-tolerance curve and the response to insulin. On the other hand, there are three things that do not fit in with Cushing's disease: The patient was still bleeding, and in Cushing's disease amenorrhea is one of the outstanding symptoms; she had an enlarged clitoris, which is not found in Cushing's disease—it does produce hirsutism without virilism; and she had low 17-ketosteroids,—about 5 mg.,—almost all cases of Cushing's disease (I think Dr. Albright will agree) having high ketosteroids, and all cases of cancer of the adrenal gland having tremendously high values, even up to 100 mg. We have these three things to explain if we say that this patient had Cushing's disease. How can we explain the enlarged clitoris? If we accept that finding, we have to explain it by some masculinizing type of tumor—adenoma of the androgenic cells of the adrenal gland or tumor of the ovary of the masculinizing type. On the second admission, the patient had pain in the pelvis, with tenderness after bleeding and with great tenderness on examination. Might there be an ovarian tumor of some type? Against this is the fact that she had been examined under ether and nothing had been felt; but one of the men in the Out Patient Department thought that he did feel a mass. If we consider the ovarian tumors that cause bleeding after the menopause—and with bleeding after the menopause ovarian tumors must always be considered—and if we also consider ovarian tumors that have endocrine activity, we have to consider three: granulosal-cell tumors, thecal-cell tumors and arrhenoblastomas. The first two are feminizing tumors and cause bleeding by

*Soskin, S. The blood sugar: its origin, regulation and utilization. *Physiol. Rev.* 21:140-193, 1941.

the overproduction of estrin, which in turn produces hyperplasia of the endometrium. At operation the endometrium was atrophic. The arrhenoblastoma is a virilizing tumor and would account for the large clitoris, but would not account for the weakness, because patients with this type of tumor are strong. It would not account for bleeding, because the virilizing tumor characteristically stops bleeding. Dr. Albright has seen one case of arrhenoblastoma in which periods went on but ovulation ceased. Arrhenoblastoma would not explain the changes in the sugar metabolism. We have on examination no evidence for a Cushing's tumor of the adrenal gland, nor have we any evidence for a tumor in the ovary. We cannot explain the bleeding and the large clitoris satisfactorily from any one point of view. There is one other possibility. This woman did have headaches. We are not told anything about the possibility of acromegaly. Acromegaly might explain the picture. We could have a diabetic curve due to insulin resistance. The ketosteroids would not be raised. We are not told about the visual fields; we are told only that the eyes were normal. We are not told about the phosphorus, which may be increased in acromegaly, nor are we told about the facies and teeth. I think that we must consider acromegaly as a possibility.

The only way that I can put this case together is as follows: It is possible that this woman was bleeding from an atrophic uterus, that she forced blood out of the tubes into the pelvis, causing a localized aseptic peritonitis, which might explain the pelvic situation. I do not see how we can explain the whole picture on the basis of ovarian tumor. The enlarged clitoris I shall have to put down as unexplained,—that she was a big woman and had a big clitoris, or the examiner was not conversant with the various sizes of the clitoris. I believe that this case fits best into the Cushing's disease group, and I should like to ask Dr. Albright if the ketosteroids are always high in that disease. If that is so, and if the ketosteroids were low normal here, I should be forced back to the hypothesis that the patient had an eosinophilic tumor of the pituitary gland.

Dr. Fuller Albright: I think we can give Dr. Fremont-Smith more information. I should like to say that the skin was not atrophic. What was the follicle-stimulating hormone test in the urine before operation?

Dr. Tracy B. Mallory: It was not done until two days after operation, when it was negative.

Dr. Fremont-Smith: That would mean that the basophilic cells were not active, as they should be after the menopause. That makes one believe there was something interfering with the basophilic cells, such as tumor of the eosinophilic cells. Is there any more information that I could have?

Dr. Albright: You have not commented on the acne.

Dr. Fremont-Smith: I wish you would comment on that.

Dr. Albright: I think Dr. Fremont-Smith has given an excellent discussion. He did not come out with the right answer any more than those who saw the patient before the operation. To one like myself, who saw her only after the diagnosis was made, it was easy to see that the findings fitted in with the correct diagnosis. The follicle-stimulating-hormone test two days after operation was negative and presumably was negative before operation. This test should be positive after the menopause unless some factor is present that inhibits its production. One of the hormones that does just this is testosterone. The fact that this test was negative, therefore, would make one go back to the possibility of an arrhenoblastoma, which produces either testosterone or, what is more likely, a testosteronelike steroid. Furthermore, testosterone does produce acne. The patient had hot flashes at one time, which is strong evidence, in my opinion, that at that time she had an excess production of follicle-stimulating hormone. It would be my interpretation that the arrhenoblastoma developed subsequent to the time when the patient was having hot flashes. It is of interest that the follicle-stimulating-hormone test, done some time after the arrhenoblastoma was removed, was strongly positive, as was to be expected.

Dr. Fremont-Smith: How about the sugar curve?

Dr. Albright: I cannot answer that. It is of interest that the glucose-tolerance test done some time after operation was perfectly normal. I do not know whether this indicates that the arrhenoblastoma had an effect on sugar metabolism, or whether the patient was not properly prepared for the first test. I am inclined to the latter interpretation. Incidentally, the glucose-insulin-tolerance tests did not show insulin resistance, as stated above.

Dr. Fremont-Smith: How about the bleeding?

Dr. Albright: I think you explained it—an atrophic uterus.

Dr. Fremont-Smith: In fairness I think I should say that I thought they operated on the uterus to get rid of the bleeding.

Dr. Mallory: The only preoperative diagnosis that they committed themselves to was postmenopausal bleeding.

Dr. Fremont-Smith: How about the ketosteroids?

DR. ALBRIGHT: In our one other case of arrhenoblastoma in which the 17-ketosteroids were measured they were found to be normal.

DR. MALLORY: But should they not be high?

DR. ALBRIGHT: They should be if the arrhenoblastoma produces testosterone. There are several steroids similar to testosterone that are masculinizing but are not 17-ketosteroids.

DR. FREMONT-SMITH: Are the ketosteroids always high in Cushing's disease?

DR. ALBRIGHT: No. However, if you take into account that most patients with Cushing's syndrome are very debilitated, a condition that in itself leads to low 17-ketosteroid excretion, I think it is fair to say that the 17-ketosteroids are either high or relatively high.

CLINICAL DIAGNOSIS

Postmenopausal bleeding.

DR. FREMONT-SMITH'S DIAGNOSIS

Cushing's syndrome.

ANATOMICAL DIAGNOSIS

Adenoma testiculare of ovary.

PATHOLOGICAL DISCUSSION

DR. MALLORY: At operation the old abdominal scar was opened up and an exploration performed. The surgeon palpated both adrenal glands and reported that they felt larger than normal, but could find no evidence of tumor in either. I think it is reasonable to question even that first statement, because my experience is that the surgeon always thinks the adrenals are larger than normal if he palpates them. One naturally visualizes the adrenal glands as they are seen at autopsy, when they contain no blood. The adrenal gland is distinctly larger in life than it is at autopsy.

The pelvis was more carefully explored, and a sharply localized tumor was found in the right ovary, which measured 3 by 2 by 2 cm., and was yellowish in color. At that point they became convinced that they were dealing with an arrhenoblastoma. Since, however, the most distressing symptom had been the uterine bleeding, they considered it wise to do a hysterectomy and get rid of the focus of bleeding, as well as to remove the ovarian tumor. In our laboratory when the tumor was examined it turned out to be the more highly differentiated form of masculinizing tumor known as the "adenoma testiculare of Pick" rather than the so-called "arrhenoblastoma." The older literature would lead one to believe that the adenoma testiculare is not a functioning tumor, but this is the second we have had in this hospital in which there was evidence of a masculinizing action.

CASE 27162

PRESENTATION OF CASE

First Admission. A sixty-five-year-old wool cutter entered the hospital complaining of burning and frequency of urination.

Three months before admission the patient cut his left leg. The lesion was slight and he continued working, but it did not heal, discharged a dirty purulent material, and gradually progressed to a deep ulcer. Pain, redness and swelling developed in the leg to a point necessitating hospitalization.

One week before admission, the patient awoke with a gripping sensation in the right chest, accompanied by a cough and a small amount of blood-streaked sputum. The sputum lasted for one day, but the chest pain continued for three days.

Four years before admission, the patient had been refused life insurance because of high blood pressure. Since that time he had noticed a progressive decrease in his exercise tolerance, so that at the time of admission he was unable to climb a flight of stairs without dyspnea. Of recent weeks swelling had appeared in the feet and ankles of both legs.

He complained also of occasional nocturia for an unstated period. He had had scarlet fever, and twenty-five years before admission "bronchial asthma" for six months. Usually he drank one or two glasses of beer each day and up until two years before admission anywhere from a half pint to two pints of whiskey a week. The patient's father had died of carcinoma of the stomach.

On examination the patient was well developed, well nourished and very drowsy. The tongue was dry, the pharynx injected and covered with a purulent exudate. The lungs were clear, the heart slightly enlarged to the left, but otherwise normal; the blood pressure was 118 systolic, 78 diastolic. The peripheral arteries were soft and pliable. The abdomen was protuberant, and the smooth, nontender liver was palpable 3 fingerbreadths below the right costal margin. Slight pitting edema of the sacrum was present. The prostate was slightly enlarged, but not of abnormal consistence. The right leg was reddened from the toes to the knee, with a sharp, but irregular line of demarcation at the normal skin border. The upper portion was hemorrhagic and did not blanch on pressure. A 4.5-cm. ulcer with a dirty base and surrounded by small pustules was present over the lower tibia.

The entire lower leg was tender and indurated without fluctuation, and the left thigh was pink and edematous, especially on its medial aspect. There was pitting edema of both lower legs, and the right lower leg showed areas of hemorrhagic discoloration. Pulsation could not be felt in either dorsalis pedis or posterior tibial arteries, but was present in the popliteals and femorals.

The temperature was 100.2°F., the pulse 82 and the respirations 23.

The urine gave a green and occasionally an orange sugar reaction. The blood showed a red-cell count of 4,650,000 with a hemoglobin of 85 per cent, and a white-cell count of 15,000 with 86 per cent polymorphonuclears. The fasting blood sugar was 127 mg., the nonprotein nitrogen 27 mg. and the protein 5.4 gm. per 100 cc. The prothrombin time was 24 seconds (normal 19), a hematocrit reading 44 per cent, the vitamin C 0.5 mg. per 100 cc.

An x-ray film of the legs showed a marked irregularity of the soft tissue about the left lower leg, with a defect anteriorly and posteriorly. There was very slight decalcification along the anterior aspect of the tibia. No periosteal new-bone formation was visible.

The patient was given sulfanilamide, intravenous fluids and digitalis, the blood sugar being controlled by diet and insulin. Cultures from the ulcers yielded *Bacillus subtilis, Proteus vulgaris* and *Staphylococcus aureus*. Two days after admission, a slight icteric tint was noted in the scleras and the serum van den Bergh at this time was 6.5 mg. per 100 cc., biphasic; sulfanilamide therapy was discontinued and a high-vitamin, high-carbohydrate and low-fat diet instituted. The patient's legs improved very favorably, and the edema subsided, but a week after admission a deep ulceration with purple margins and dirty base developed in the left calf and two days later was found to communicate with a collection of pus between the muscle planes; this was incised and drained under local anesthesia. Subsequently a carbuncle of the left buttock appeared, and excision was necessary. Under treatment the patient slowly improved, and the ulcers healed with the aid of pinch grafts. The diet was readjusted to combat the hyperglycemia, and the patient was discharged eight weeks after admission, at which time the serum van den Bergh was 2.0 mg. per 100 cc., biphasic, and a bromsulfalein test showed 10 per cent retention of the dye. The last urine specimen, recorded three weeks before discharge, was negative, and 28 previous specimens had contained no sugar.

Final Admission (seventeen days later). Shortly after leaving the hospital, the patient began to have urinary difficulties in the form of hesitancy, frequency with large quantities voided, and a slow, weak stream. In addition, there was burning, and nocturia thrice a night. He denied hematuria, chills, fever, nausea or vomiting. For the previous week he had suffered from a nonradiating, dull, aching pain in the left flank and costovertebral angle. Two days before admission, he was unable to void and was catheterized by his physician.

On examination the patient was drowsy and in moderate distress. The heart and lungs were essentially normal, the blood pressure 130 systolic, 85 diastolic. There was exquisite tenderness, bulging and spasm in the left costovertebral angle; the liver was palpable three fingerbreadths below the costal margin. The prostate was greatly enlarged, smooth, symmetrical and firm. Peripheral edema was not present.

The temperature was 101.5°F., the pulse 72, and the respirations 20.

The urine showed a +++ test for albumin and was loaded with white blood cells and bacteria; a culture yielded abundant colonies of nonhemolytic streptococci and *Staph. albus*. The blood showed a red-cell count of 3,400,000 with a hemoglobin of 60 per cent, and a white-cell count of 38,900 with 96 per cent polymorphonuclears. The fasting blood sugar was 142 mg., the nonprotein nitrogen of the serum 45 mg., the protein 5.8 gm. per 100 cc., the chlorides being 83.5 milliequiv. and the carbon dioxide combining power 26.6 milliequiv. per liter. A phenolsulfonephthalein test showed 7 per cent excretion of the dye in two hours.

An intravenous pyelogram was unsatisfactory, owing to marked respiratory motion on all films. The colon was markedly distended with air and appeared slightly dilated down to the sigmoid; the rectum was not dilated. No filling of the kidneys was visible on any of the films, and no dye was seen in the bladder at the end of forty-five minutes. An electrocardiographic recording showed a normal rhythm at 100 and a PR interval of 0.17 second. There was marked left-axis deviation, S_2 was deep, ST segments were slightly depressed in Lead 1 and elevated in Lead 3 and T_1 was biphasic.

Slow decompression of the bladder was carried out, and chemotherapy and intravenous fluids, guarded by insulin, given. On the third hospital day the prostate was found to be tender and fluctuant, so that a perineal drainage of the abscess was performed; a culture of its purulent contents yielded *Staph. aureus*. Throughout hospitalization the patient was stuporous and toxic, respiration became labored, the temperature rose to 102°F. and the pulse to 110. One week after admission

the nonprotein nitrogen was 90 mg. per 100 cc., the chlorides 91.7 milliequiv. and the carbon dioxide combining power 21.8 milliequiv. per liter. A flat abdominal film showed apparent thickening in the soft tissues in the region of the right psoas muscle, and the left psoas muscle was but faintly visualized. An x-ray film of the chest taken with a portable machine showed poor aeration of both lower lung fields, more marked on the left side, where there was definite evidence of consolidation consistent with pneumonia. Two days later cystoscopic examination was performed. The bladder mucosa was pale, lackluster and edematous, and the ureteral orifices were edematous. Catheters were passed to both kidneys, and this was followed by hydronephrotic drips from both. The culture from the left kidney yielded *Staph. aureus,* that from the right, a moderate growth of nonhemolytic streptococci. Finally the patient became comatose and dyspneic, edema developed to the scrotum, and the nonprotein nitrogen rose to 100 mg. per 100 cc. Death occurred two weeks after admission.

Differential Diagnosis

Dr. Champ Lyons: Dr. Bland, can you give us an interpretation of these electrocardiographic hieroglyphics?

Dr. Edward F. Bland: Yes; it is an abnormal record, the chief thing being left-axis deviation, which suggests some cause for strain on the left ventricle. The ST changes are, however, secondary to the axis deviation.

Dr. Lyons: Dr. Hampton, should you like to comment on the x-ray films now?

Dr. Aubrey O. Hampton: I am not very proud of these films. They all show motion. The patient was apparently unable to co-operate, and all the statements made in the record are probably based on insufficient evidence.

Is there anything that interests you very much?

Dr. Lyons: I am particularly interested in the interpretation of the consolidation in the lungs.

Dr. Hampton: As you can see, it is rather difficult to tell whether there is anything there or not. There is always more density along the left border of the heart when there is motion, and we may be making the mistake of calling that shadow pneumonia. I should think there is an area of consolidation in the left lung near the border of the heart. Small lesions diffusely scattered over the lung are not ruled out.

Dr. Bland: Is the left ventricle full?

Dr. Hampton: Yes; the heart appears enlarged, particularly in the region of the left ventricle. I was trying to find the best film here of the psoas-muscle shadows. They were apparently interested in the psoas muscles. The upper parts of both muscles are distinct. The lower portions fade out, but I do not believe we have enough evidence to suggest a psoas abscess. The kidneys appear large, and they do not function, as indicated by intravenous pyelogram.

Dr. Lyons: This is the record of a sixty-five-year-old wool cutter with a progressive infection. His occupation suggests the possibility of anthrax, but all the cultural evidence indicates a staphylococcal infection.

Of interest in the past history are the stories of alcoholism, scarlet fever and progressive symptoms of heart failure during the last four years.

The immediate history is one of a neglected traumatic wound of the leg, which failed to heal, discharged pus, became ulcerated, and developed areas of hemorrhagic discoloration. One week before entry the patient suffered what I have interpreted as a pulmonary infarct.

On entry to the hospital he was dehydrated, with mild congestive failure and mild diabetes. A culture of the leg wound revealed *Staph. aureus* as the most probable pathogen. The absence of arterial pulsations in both lower extremities was indicative of peripheral arteriosclerosis and circulatory failure. The irregular but sharply demarcated zone of redness and hemorrhagic discoloration that did not blanch on pressure is of real interest. This is not the picture of erysipelas; the cultures failed to show a hemolytic streptococcus, and the patient should not have been very sensitive to erysipelas toxin because of the history of scarlet fever. The blood Hinton reaction is not reported, but tertiary syphilis is not a satisfactory explanation of this picture. A normal blood cevitamic acid and prothrombin time and an absence of purpuric spots elsewhere make it likely that the skin changes were of local origin. I have interpreted these changes as the result of a venous thrombosis in an extremity with circulatory deficiency. This offers a logical explanation of the source of the pulmonary infarct described in the history and permits a hypothetical reconstruction of the course of events that led to the patient's death. I have reasoned that the thrombophlebitis was a septic staphylococcal thrombophlebitis and gave rise to the staphylococcemia necessary for the development of metastatic visceral abscesses present at the time of the second admission.

The enlarged liver and the development of jaundice after two days of sulfanilamide are extremely interesting. If the liver enlargement were on the basis of congestive failure, I should have expected it to be tender and associated with signs of pulmonary congestion. Amyloid disease does not ap-

pear likely because of the short history of sepsis. The history of alcoholism suggests that there may have been an alcoholic type of toxic cirrhosis. Jaundice developed coincidentally with the use of sulfanilamide and digitalis, and I believe that this was a toxic hepatitis in a cirrhotic liver.

At the time of the second admission the patient presented the problem of multiple abscesses and renal failure. A staphylococcal abscess of the prostate was drained, and the clinical signs of perinephric abscess on the left were present. The x-ray picture of consolidation was probably produced by septic pulmonary infarcts, which could have come from the prostatic venous plexus but more probably from the veins of the right leg. The blood culture post mortem should be positive for staphylococci. The location of other abscesses is largely a matter of conjecture on a statistical basis. There is no evidence in the record to establish a diagnosis of endocarditis, brain abscess or vertebral osteomyelitis. One or more small myocardial abscesses are extremely likely. My final diagnoses are: staphylococcemia; extensive septic thrombophlebitis arising from the veins of the right leg; septic pulmonary infarcts; abscesses of the kidneys, heart and prostate; peripheral arteriosclerosis and arteriosclerotic heart disease; toxic cirrhosis of liver — alcoholic type; mild diabetes mellitus; and healed ulcer of leg.

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Clinical Diagnoses

Cellulitis of left leg.
Carbuncle of buttocks.
Prostatic abscess.
Acute pyelonephritis.
Uremia.
Cirrhosis of liver.
Arteriosclerotic heart disease.

Dr. Lyons's Diagnoses

Staphylococcemia.
Extensive septic thrombophlebitis arising from the veins of the right leg.
Septic pulmonary infarcts.
Abscesses of the kidneys, heart and prostate.
Peripheral arteriosclerosis and arteriosclerotic heart disease.
Toxic cirrhosis of liver, alcoholic type.
Mild diabetes mellitus.
Healed ulcer of leg.

Anatomical Diagnoses

Staphylococcal septicemia with abscesses in prostate, kidneys and lungs.
Ulceration of left lower leg.
Septic thrombophlebitis, left leg.
Septic infarction of the lungs.
Hypertrophy of the heart.
Biliary cirrhosis of the liver.
Cholelithiasis.

Pathological Discussion

Dr. Tracy B. Mallory: At the time of autopsy the major sepsis was localized in the kidneys. Both kidneys were very considerably enlarged and were studded with innumerable soft and large abscesses that had almost completely destroyed the parenchyma. I think the immediate cause of death was probably renal insufficiency rather than sepsis, although unquestionably both must have played a role. There were areas of septic infarction, with definite abscess formation in the lungs. The heart was enlarged, without an intrinsic lesion. The coronary arteries for his age were in quite good condition. I should think there was very little doubt that the hypertrophy went back to his known hypertension of many years' duration.

The liver was normal in size, and showed no evidence of abscess formation or chronic alcoholism. There was none of the fatty vacuolization that usually precedes an alcoholic cirrhosis. On the other hand, there was very slight but definite cirrhosis, and this was of the biliary type. There was proliferation of bile ducts and a significant inflammatory infiltration of the periportal connective tissue. Nothing in the history suggested gallstones, but the gall bladder did contain numerous faceted stones, and I should think that at some time in the past the patient must have had one or more stones in the common duct that caused some degree of obstruction and perhaps some retrograde infection. There was a considerable degree of inflammatory infiltration of the perinephritic tissues on both sides, a little more marked on the right, without, however, any frank perinephritic abscess. We were unable to determine the source of the septic emboli to the lungs. They might have come from either the leg vein or the periprostatic plexus. The sections showed a great many clusters of organisms resembling staphylococci in both lungs and kidneys.

Dr. Hampton: I should like to ask if anyone would consider ligating that vein if this situation occurred again.

Dr. Lyons: I should like to point out that, when the vein originally thrombosed, hemorrhagic discoloration appeared. We have done femoral-vein ligation for thrombosis in this age group without changing the course of events. The last patient died of gas-bacillus infection with necrosis.

Dr. Benjamin Castleman: Your objection to ligation would apply only to septic phlebitis?

Dr. Lyons: Yes.

The New England
Journal of Medicine

Formerly the
Boston Medical and Surgical Journal
Established in 1828

Owned by the Massachusetts Medical Society and Published under the Jurisdiction of the Committee on Publications

Official Organ of
The Massachusetts Medical Society
and
The New Hampshire Medical Society

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Subscription Terms: $6.00 per year in advance, postage paid, for the United States; Canada, $7.04 per year, Boston funds; $8.52 per year for all foreign countries belonging to the Postal Union.

Material for early publication should be received not later than noon on Saturday.

The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston, Massachusetts.

IN MEMORIAM: FREDERICK GRANT BANTING — EDWIN NELSON CLEAVES

Frederick Grant Banting, born on November 4, 1891, at Alliston, Ontario, was graduated in medicine from the University of Toronto in 1917 and soon was awarded the Military Cross for attending the wounded under fire at Cambrai, France. The world knows of his collaboration with a medical student, Charles H. Best, in the laboratory of Professor McLeod at the University of Toronto, of their joint discovery of insulin, announced in 1922, and of Banting's insistence that his half of the Nobel Prize, awarded in 1923, be shared with his co-worker, Best.

Known only to a small group is the Boston story, that of Edwin Nelson Cleaves, born in Medford, Massachusetts, in 1890, and graduated from Harvard College in 1911 and from the Harvard Medical School in 1915; following graduation he was a surgical house-officer at the Massachusetts General Hospital.

It was while a house-officer, in 1916, that Cleaves, short of stature but of good physique, former captain of the Harvard Gymnastic Team, one hundred and forty pounds at his best weight, first discovered that he was excreting sugar. Becoming sugar-free on a comparatively liberal diet, he was resident and superintendent of the Out Patient Department of his hospital until the fall of 1918, when the great epidemic of influenza overwhelmed him. From that time on, his tolerance shattered, he existed on less than a thousand calories a day, weighing ninety-three pounds in his clothes when he went west in June, 1919.

In 1922 he was back in Boston, presumably for the last time, weighing eighty-three pounds, so weak that he had to be carried from his Pullman berth to the waiting stretcher. His books were audited and his accounts closed. He had fought a good fight and lost, although for months he had refused to acknowledge defeat.

At this point the lives of Banting and Best and of Cleaves met, and from then on his life was inseparable from their lives and accomplishments, for he received insulin and was among the first to be plucked by it from the grave's very brink. With health and vigor restored he returned to the fight and entered the field of roentgenology, became a member of various societies and made his own contributions to the science and the art of healing; he found relaxation and further service in work among the boys of Trinity Church. He, also, has appropriately been called a "hidden servant"; hidden only because of the narrow circle of his professional acquaintance.

Banting, continuing his scientific career, was knighted by King George V in 1934, re-entered the army, helped to establish Canadian blood banks and made important contributions to aviation medicine. Flying on a secret war mission to Britain he fell with his plane and companions, and died

in the snows of Newfoundland on February 21, 1941.

Three days later, Cleaves went to join his particular savior, working almost to the last, the victim of a nondiabetic disease, and the victor over diabetes for more than twenty-five years.

EARLY DIAGNOSIS OF TUBERCULOSIS

THE nation-wide Early Diagnosis Campaign being held throughout April by the National Tuberculosis Association and its affiliated state and local associations deserves the serious attention of every person who appreciates the need of conserving life, time, energy and money in these fateful days. Early diagnosis means a saving in lives and money. Since most cases of tuberculosis are taken care of in tax-supported institutions, and since it may take years to restore a patient with advanced tuberculosis to health,—if, indeed, cure is possible,—hospitalization of advanced cases results in a tremendous burden on the community; whereas, the early case usually is easily cured in a short time at a small cost. Year after year the public must be stirred up and made aware of the continuing threat of tuberculosis, which has lost none of its power to destroy or handicap the patient, although many fewer persons are threatened each year.

Since it is difficult to sustain interest and support in day-after-day efforts to educate the masses of people, it is well to concentrate effort and interest in a particular month. When people hear tuberculosis discussed on the radio, read articles about it in national magazines and local newspapers, and learn important facts about it from exhibits in store windows, they begin to realize that this disease is still a very serious menace. Complacency is displaced by interest and understanding and a better attitude toward the problem.

In addition to the literature provided by tuberculosis associations this year for various groups of the general public, including community leaders, educators, young, middle-aged and old people, and factory workers, a new publication is available to physicians. This brochure, entitled *Chest X-Ray Interpretation*, was written by Dr. J. Burns Amberson, Jr., and has been published by the National Tuberculosis Association.

The theme for this year's campaign is, "A Good X-Ray is Your Doctor's Best Aid in Discovering Early Tuberculosis." This slogan should lead both those who suspect they have tuberculosis, and those who have no symptoms but want a thorough health check-up, to go to their physicians with the expectation that chest x-ray films will be taken.

The present development of technics and equipment for mass x-ray studies with less expensive film hastens the time when apparently healthy persons will be examined in large numbers. Until such time, education must be relied on to convince people who most need x-ray study that they should use existing services.

OBITUARY

GEORGE LINCOLN WALTON

1854–1941

In the death of George Lincoln Walton on January 17, the Boston Society of Psychiatry and Neurology lost its oldest living member. Dr. Walton's name is doubtless only a memory to most of those present, for he ceased practice in 1916; even to the writers his early activities are shrouded in tradition, and acquaintance was based more on the happy philosophy that radiated from him in social contact, than on factual discussion in the clinic.

Dr. Walton's early interests in neurology were varied. At the turn of the century, the neurologist was equally interested in the functional and the organic diseases of the nervous system. His papers, of which there are three large volumes at the Harvard Medical School, show an interest in both, but emphasize especially structural diseases and their diagnostic signs. Even in 1900 a paper written in collaboration with Dr. W. E. Paul, commending, on the basis of much clinical study, the value of the Babinski reflex, was a novelty. His successful attempts at localization of tumors of the brain and spinal cord are duly registered, and his usefulness to the surgeon is apparent. A letter from the elder John Homans in reminiscent vein denotes the significant relation of neurologist and surgeon of that time: "I remember your dancing round the operating room—I swear it—and saying that you had waited twenty-five years for this moment, that you had made diagnoses and that no surgeon could take the tumor out."

Perhaps his main contribution to structural neurology concerns dislocation of the cervical vertebrae and the manipulation that he devised for reduction; this was in the days of observation and palpation, with no help from x-ray films.

Many of Dr. Walton's early papers deal with hysteria. Doubtless his name is most closely linked with three small popular books on psychotherapy. Many a person received help from these simple, often whimsical, yet erudite treatises on the various aspects of psychoneurosis, and one at least — *Why Worry* — ran to twenty-three printings. Those were the days of exhortation, of reasoning and of reassurance. Psychoanalysis had not been heard of, and when it came was not approved by Dr. Walton.

But it is as a happy man of resource that we like to think of him: always eager, always courteous and helpful both in word and deed. His retirement from active practice in 1916 at the age of sixty-two gave him, unlike most men, the time he had looked forward to for the hobbies that he had always advocated for others. During the subsequent twenty-five years these avocations embraced many intellectual fields, in two of which Dr. Walton became more than an amateur. He collected old silver, some pieces of which are now in the Museum of Fine Arts; he became an excellent photographer; he studied certain aspects of archaeology and gave to the Warren Museum an exhibition illustrating burial customs of ancient Egypt. History, especially historical facts, intrigued him, and his writings give evidence of this interest. A botanical work *The Flower Finder,* first published in 1914, went through four editions to 1935, and is still an approved guidebook, based on his own classification — that of color rather than of family.

With all his scientific and cultural interests, his wit, as shown in his conversation and in his writing, runs throughout, and his occasional poems, read before gatherings of the American Neurological Association and of the Chakara Club and elsewhere, disclose the gay yet serious qualities of his mind.

Dr. Walton's death breaks a link with our intellectual past. We mourn this fact. We acclaim his success.

C. A. M.
J. B. A.

MEDICAL EPONYM

Henle's Loop

This anatomic structure was described by Friedrich Gustav Jacob Henle (1809–1885), professor of anatomy at Göttingen in his *Handbuch der systematischen Anatomie des Menschen* (Vol. II, p. 303; Braunschweig, 1862). A portion of the translation follows:

> The narrow canaliculae are always found in the interstices between the larger ones, running parallel with them and showing no tendency whatever to join them. Instead, they terminate at various levels, the lowest immediately under the surface of the papillae in the bridges between the larger canals, and are blind in the sense that two neighboring canaliculae join together in a sharp loop. Because of this course I have given them the name of loop-shaped canaliculae.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON STATE AND NATIONAL LEGISLATION

House Bill 1477, the enabling act for medical-costs insurance sponsored by the Society, has been passed by the Committee on Insurance, and the House Counsel has written an emergency preamble to the bill. It has received a new number, becoming House Bill 2301, and has been sent to the House Committee on Ways and Means. No date has yet been set by that committee for a hearing on the bill, but all members of the Society should get in touch with members of that committee who are from their districts and ask them to act favorably and promptly on the bill. The list of members of the House Committee on Ways and Means, with their addresses, appeared in the March 20 issue of the *Journal.* All representatives and senators not on the committee should be requested to appear before the committee and register their approval of the bill.

Henry C. Marble, *Chairman.*

SECTION OF OBSTETRICS AND GYNECOLOGY*

Raymond S. Titus, M.D., *Secretary*
330 Dartmouth Street
Boston

Hypertension Associated with Pregnancy and Resulting in Premature Delivery and Fatal Post-Partum Convulsions

A twenty-nine-year-old para IV was first seen very early in her pregnancy by her family physician. At that time her blood pressure was 180 systolic, 110 diastolic, and her weight was over 200 pounds.

At fourteen years of age, the patient had had a

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

blood pressure of 190 systolic. There was no history of scarlet fever or of kidney disease. The first pregnancy resulted in a normal delivery of a living child, the second and third pregnancies were terminated by miscarriage.

Physical examination at the time of her first visit was negative except for the aforementioned blood pressure and obesity. The lungs were clear and resonant; there were no rales. A therapeutic abortion was advised and refused.

The patient was seen routinely and was put to bed when five months pregnant. During this time her blood pressure ranged between 200 and 180 systolic, 120 and 110 diastolic. She started in spontaneous labor when she was just over eight months pregnant and delivered normally a living child. One hour later the first of five convulsions occurred, and three and a half hours after delivery the patient died. The baby died a week later of prematurity.

Comment. This is a case of hypertension, probably nephritic in origin and of at least fifteen years' duration, which resulted in premature birth and post-partum convulsions. Whether these convulsions could be called eclampsia or whether they were uremic convulsions due to an underlying chronic nephritis is debatable. The usual case of eclampsia develops in women who have normal blood pressure at the beginning of pregnancy.

Hypertension of this degree — 200 systolic, 120 diastolic — at the onset is a grave condition, and conservatism indicates the interruption of pregnancy. In this particular case, the suggestion of interruption was made, but the patient refused. She was treated adequately with rest in bed after the fifth month; frequent urinalyses were carefully carried out, and a proper diet was prescribed, but the outcome was only what one might have expected.

Premature labor is a common occurrence in cases of hypertension. Intrauterine death frequently precedes premature labor, and when this occurs the patient often improves symptomatically. Obstetrically, it might have been wise to have delivered this woman as soon as it was believed that the baby was viable. The possibility of her going to term and surviving with a blood pressure of this sort from the beginning was extremely unlikely.

MEDICAL POSTGRADUATE EXTENSION COURSES

The following sessions, given by the Massachusetts Medical Society in co-operation with the Massachusetts Department of Public Health, the United States Public Health Service and the Federal Children's Bureau, have been arranged for the week beginning April 20:

BERKSHIRE

Thursday, April 24, at 4:30 p.m., in the Bishop Memorial Building, Pittsfield. Obstetric Infections: Diagnosis and treatment. Instructor: Joseph W. O'Connor. Harry G. Mellen, *Chairman.*

BRISTOL SOUTH (Fall River Section)

Tuesday, April 22, at 4:30 p.m., at the Union Hospital, Fall River. Diagnosis and Treatment of Minor Lesions of Rectum and Anus. Instructor: Franklin G. Balch, Jr. Howard P. Sawyer, *Chairman.*

FRANKLIN

Thursday, April 24, at 8:00 p.m., in the Library of the Franklin County Public Hospital, Greenfield. Acute Abdominal Pain: Its interpretation and management. Instructor: Stanley J. G. Nowak. Halbert G. Stetson, *Chairman.*

HAMPDEN

Wednesday, April 23, at 4:00 p.m., at the Academy of Medicine, Professional Building, 20 Maple Street, Springfield, and at 8:00 p.m., in the Outpatient Department of the Skinner Clinic, Holyoke Hospital, Holyoke. Pediatric Case Discussions. Instructor: Edwin H. Place. Alfonso A. Palermo, *Chairman.*

HAMPSHIRE

Thursday, April 24, at 4:15 p.m., in the Nurses' Home of the Cooley Dickinson Hospital, Northampton. Therapeutic Uses of Preparations of Endocrine Glands: Thyroid gland, pituitary gland, ovary, testis and adrenal cortex. Instructor: Harry B. Friedgood. Robert C. Byrne, *Chairman.*

WORCESTER

Tuesday, April 22, at 8:30 p.m., in the Nurses' Home of the Milford Hospital, Milford. Chemotherapy in the Treatment of Gonococcal Infection. Instructor: Weston T. Buddington. Joseph Ashkins, *Chairman.*

WORCESTER NORTH

Friday, April 25, at 4:30 p.m., in the Nurses' Home of the Burbank Hospital, Fitchburg. Dermatitis and Eczema. Instructor: Mildred L. Ryan. George P. Keaveny, *Chairman.*

THE EGO: NERVES AND SELFISHNESS*

Mental hygiene, maladjustment, "nerves" and nervous breakdowns are so much talked about and written about these days that we may well be somewhat bewildered in trying to understand and to know what to believe. Most of us have become more and more conscious of the fact that we can feel nervous, unhappy or even sick without any physical disease. We are told that our emotions or mental conflicts can cause nervousness in its many forms. And furthermore we are advised that we may not even be aware of what is making us nervous, because the seat of our troubles may be in our unconscious minds. Unconscious or subconscious desires or conflicts are pointed to

*A "Green Lights to Health" broadcast given through station WAAB by Dr. Vernon P. Williams on Wednesday, January 29, and sponsored by the Public Education Committee of the Massachusetts Medical Society and the Massachusetts Department of Public Health.

as the origin of our jitters, our gloomy moods, our restlessness, unhappiness and so forth.

Now, this so-called "discovery" of modern science — that unconscious motives may be responsible for the way we act and the way we think and feel — can be quite disturbing if not frightening. We may be at a loss to know what awful forces or ideas have us in their power, and even if we try to find out we may not be sure that we have the right answer.

In maintaining or regaining a reasonable degree of mental health, it may not always be necessary to ask for the aid of a specialist in psychology. Even though it is true, as it certainly is, that we can get into trouble because of motives and tendencies of which we may be unaware, we should not let ourselves off too easily with the partially comforting thought that we are not responsible because we are in the grip of our mysterious unconscious minds. If we are willing to face the facts, — and it is healthy to do so, — we can frequently see wherein our difficulties lie.

Today the subject to be discussed is related to one very important part of the structure of the human personality — a part that is so obviously present in all of us that it should not require the expert help of a psychiatrist to make us aware of its existence. It is powerful and forceful, and we may not always be aware of its presence and yet even a moderate amount of self-examination by a person of average intelligence will convince us that the depths of human personality do not have to be plumbed to discover it. This part of us may be called "the ego."

You know that in all of us there are deep, instinctive drives or forces that have to do with our well being. We have bones to support the other tissues of our bodies. We have hearts to pump the oxygen-carrying blood through our bodies, and we have instinctive forces, which in complicated ways enable us to adjust ourselves to and hold our own in an external world that makes all sorts of demands on us. Now what is called the ego is the urge to protect ourselves and to make our way through life with as little harm or injury to ourselves as possible. It is the same force that makes the housefly try to avoid the swatter or the bird in the street avoid the oncoming automobile. But it is more than that: it is also the force that inclines us to get as much as we can for ourselves. It gives us our ambition, our desire to excel or at least to be as good as anybody else in the many situations that develop from our contacts with other human beings. It is the force that tends to make us see ourselves in as favorable a light as possible and to close our eyes to our shortcomings. And sometimes, unfortunately, it is the force from which comes an insatiable craving for power. I refer not only to a would-be world conqueror, but also to anyone who does not have the sense to limit his desires for dominance or pre-eminence in all the various directions in which his interests may lie.

Now, this ego drive or force is surely behind much of our behavior, and is consequently related to some of our deepest feelings and motives. One may say, "What of it? Isn't it good and natural to want to protect and develop oneself?" Of course it is, but the trouble is that unless this ego drive is controlled by reason and intelligence, it may get out of hand and lead us into difficulties. And one of the common difficulties is nervousness in some form or other.

If we have become accustomed to obtaining what we want and then at a certain point find that our aggrandizing desires are blocked because of circumstances or because they come into conflict with what other people want, we are apt to feel frustrated and unhappy unless we have the judgment to know that it is good that there should be a limit to our egotistic advances. And it is a fact that nervous symptoms may arise when we feel frustrated.

It is easy for us to see the importance of checking this ego drive when we are considering other people. We all know that it is common sense to curb a selfish child before he develops tantrums when he cannot have what he wants. It may not be quite so easy to see selfishness in ourselves when we are upset because our wives or husbands are not so considerate of us as we think they should be. When we are offended, it is wise to consider whether or not we too may sometimes say or do things that may be displeasing. Also we might keep in mind the possibility that we may be unhealthily sensitive or that the person who makes unpleasant remarks may himself be suffering from a maladjustment that will not be cured by counterattack.

We are inclined to be so self-protective that unless we are wise or big-hearted or generous in our feelings toward other people we react instinctively to being rubbed the wrong way. If we are offended, insulted or neglected by anyone whose attitude affects us, the tendency is to hit back, to become resentful, to bear a grudge or to brood gloomily over the offence. This is no recent discovery. Christ pointed it out when he made the suggestion about turning the other cheek. Even that fictitious creature, the cold-blooded scientist, is not immune to this self-protective reaction. It is natural to respond to and to feel friendly toward people who respond to us, or who at least do not step on our particular mental corns.

We may or may not be aware of it, but one of our first reactions in meeting people is to sense whether or not they like us or give us due consideration. Many a friendship of years' standing, founded perhaps on not too solid a basis, may be threatened or broken by a too-frank criticism of our weaknesses. Someone has said that one sign of being a mature person is having the tact not to tell our friends things about themselves that we know they do not want to hear.

Such is the nature of the ego that the memory of a slight or a hurt may continue for years. On certain occasions, — when the warmth of friendliness or sometimes the warmth of alcohol, may induce it, — one person may tell another that the only thing he has ever held against him was the time when he said thus and so — always a body blow to his self-esteem.

We do not like to think of our frailties, and we are not likely to welcome other people bringing them up for discussion. It is, of course, not healthy to be morbidly introspective, to brood over one's shortcomings, and it is not suggested that we follow such a pursuit. But it is well to consider whether or not our egos, our selfish aims, may not need investigating when we find that we are in trouble with ourselves, other people or our environments. The selfish person is not inclined to spend much time thinking of his selfishness; if he were, he might try to do something to correct it. However, one need not be predominantly selfish to have ego trouble in some direction. A man may be quite unselfish toward his wife and children and yet be jealous of someone with whom he thinks he is in competition in his office. Or he may be entirely too possessive with his wife or children and nevertheless have a very fair and co-operative spirit with his business associates. It is interesting to note that the seventeenth century French writer, the Duke de la Rochefoucauld, whom Byron called "Nature's sternest painter, yet the best," saw so piercingly into the human ego that his writings were at various times suppressed.

The self-protective ego manifests itself in many ways.

Sometimes we see it in the form of gossip or criticism of other people. The criticism is frequently of people whom we know in our hearts to be superior to us in certain respects, or of people who have done us a hurt. The criticism is a cheap leveling process by which we try to compensate for our feelings of inferiority.

Now perhaps all this sounds too simple, too obvious. After all, everyone knows that those who live in glass houses should not throw stones — this was said, of course, before the invention of the substantial, modern glass house. Everyone knows that we are more likely to see the mote in our brother's eye than to be aware of the beam in our own. But let us not be too sure that the things that are obvious can be dismissed as lacking in profundity. In modern scientific investigation of the human mind there is too often a tendency to discard the obvious as being superficial. And yet up to the present, science has discovered nothing more fundamental than the human ego.

Even the sex impulse has not been proved to be so important. It is claimed by some investigators of human behavior that some maladjustment of the sexual instinct is always the primary cause of neurotic difficulties. This can scarcely be so when we know that two people may like each other tremendously, although not at all attracted sexually. Also, it is a fact that many husbands and wives who are not particularly compatible sexually have happy and on the whole satisfactory married lives. If two people care enough about each other and about something beyond their own physical satisfaction, they can have a good and contented life together in spite of lack of sexual compatibility.*

It is true that sexual frustration, together with frustration of the desire for just the right amount and kind of affection and understanding, can be very hard to face calmly and cheerfully, and yet if we do not have it in our heads, through overemphasis, that we must have this satisfaction, we can go along very well; it has been done again and again.

It should not be concluded from this discussion of the ego that a meek, self-effacing attitude is healthy or desirable. Some people give in too easily. They do not assert themselves enough, and there are always others who take advantage of those whom they can dominate. But analysis of people's difficulties shows repeatedly that a person can become nervous and unhappy because of a thwarting or frustration of his wants and desires. If we stop to think that we cannot have everything we want and cannot expect other people to be entirely as we should like to have them, the insight gained will help to dispel the emotional upheaval that is making us sick.

There need not be anything especially mysterious or unfathomable in many of our troubles if we are willing to do a little self-examination. If we are having ego trouble in relations with other people, the secret is to go a few steps farther than the other person in self-criticism, tolerance and understanding, rather than become aggressive or resentful.

* * *

Q. If we are as self-protective as you suggest, I should think it would be very difficult for us to admit that our troubles are due to egotism.

A. It may well be. People differ greatly in how willing they are to be frank with themselves, and again, so powerful and blind may the ego be that it seems practically impossible for some to admit that they may be wrong. But the ego drive does not have to be self-destructive. Since its very nature is to protect the personality through intelligence and reason, this protection can be farsighted and wise. Willfulness of the moment can be sacrificed for healthy gain in the long run.

Q. Would it be called selfish to strive to do one's best in one's work or profession and not to give in to obstacles?

A. Not necessarily, but it is wise to remember that we all have limitations, and if nervous symptoms develop along with our striving we should consider whether or not egotistic ambition is impelling us beyond our abilities.

Q. In relations between people, I should think it would be hard to know when it is right to assert oneself so that one is not being stepped on, and when one should tolerantly hold one's tongue.

A. That should depend on whether one is hitting back because some weakness in oneself, which one does not like to face, has been touched, or whether the offending statement is objectively untrue. Most frequently the soft answer is good policy. Notice that policemen frequently quiet down when their outbursts do not get an angry response. We should be able to have an inner strength and self-possession founded on adequate self-knowledge. Hitting back with words or acts is then much less likely to occur, and that would in no way be a sign of moral or character weakness.

*This and the subsequent paragraph were omitted in the broadcast.

MISCELLANY

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR FEBRUARY, 1941

Diseases	February 1941	February 1940	Five-Year Average*
Anterior poliomyelitis	0	2	0
Chicken pox	1103	1705	1463
Diphtheria	6	13	16
Dog bite	537	630	566
Dysentery, bacillary	12	41	15
German measles	89	60	141
Gonorrhea	282	291	369
Lobar pneumonia	463	579	695
Measles	1896	1191	2360
Meningococcus meningitis	8	5	12
Mumps	696	668	1043
Paratyphoid B fever	4	1	1
Scarlet fever	531	509	941
Syphilis	344	405	429
Tuberculosis, pulmonary	192	179	184
Tuberculosis, other forms	13	30	22
Typhoid fever	3	5	5
Undulant fever	5	4	3
Whooping cough	931	532	828

*Based on figures for preceding five years.

RARE DISEASES

Anthrax was reported from: Malden, 1 (delayed report); total, 1.

Diphtheria was reported from: Chelsea, 2; Natick, 1; Peabody, 1; Rehoboth, 1; Waltham, 1; total, 6.

Dysentery, bacillary, was reported from: Belmont, 4; Danvers, 3; Cambridge, 1; Holliston, 4; total, 12.

Infectious encephalitis was reported from: Attleboro, 1; total, 1.

Malaria (therapeutic) was reported from: Foxboro, 5; total, 5.

Meningococcus meningitis was reported from: Barnstable, 1; Boston, 1; Fairhaven, 1; Groton, 1; Hopedale, 1; New Bedford, 1; Northbridge, 1; Waltham, 1; total, 8.

Paratyphoid B fever was reported from: Chelmsford, 1; Norwood, 1; Salem, 2; total, 4.

Pellagra was reported from: Boston, 2; total, 2.

Septic sore throat was reported from: Bernardston, 3;

Boston, 9; Chelsea, 1; Fall River, 2; Holyoke, 1; Lynn, 1; Medford, 1; Merrimac, 1; Newton, 1; Norfolk, 1; Peabody, 1; Revere, 2; Winchester, 1; Wrentham, 1; total, 26.

Tetanus was reported from: Concord, 1; total, 1.

Trachoma was reported from: Boston, 2; Cambridge, 1; Springfield, 1; total, 4.

Trichinosis was reported from: Boston, 1; Framingham, 4; Southbridge, 1; total, 6.

Typhoid fever was reported from: Boston, 1; Cambridge, 1; Medford, 1; total, 3.

Undulant fever was reported from: Brockton, 1; Montague, 1; Palmer, 1; Reading, 1; Wayland, 1; total, 5.

Undulant fever, paratyphoid B fever, tuberculosis (pulmonary) and whooping cough were reported above the five-year averages.

Chicken pox was reported at the lowest figure since the corresponding month in 1932.

Diphtheria hit a record low figure for February.

Dog bite was reported at the lowest figure for this month since 1938.

German measles, gonorrhea, measles, meningococcus meningitis, mumps, scarlet fever, tuberculosis (other forms) and typhoid fever were reported below the five-year averages.

Lobar pneumonia showed a record low figure for the month.

NOTICES

BOSTON CITY HOSPITAL ALUMNI DAY

Boston City Hospital Alumni Day will be celebrated on Saturday, April 26.

PROGRAM

10:30 a.m.–12:30 p.m. Dry clinic, Cheever Amphitheater.
Carcinoma of the Large Bowel and Rectum. Dr. Frank H. Lahey.
Some Bizarre Forms Taken by Contagious Diseases. Dr. Edwin H. Place.
Progress in Gynecology and Obstetrics. Dr. Frederick L. Good.
Enlargement of the Spleen. Dr. William B. Castle.
Nature and Treatment of Pulmonary Edema. Dr. Soma Weiss.
12:45 Luncheon at the hospital.
7:00 p.m. Dinner at the University Club.
Professor Bruce Hopper, of Harvard University, will be the guest speaker.

In the afternoon, there will be a choice of seeing the Red Sox game at Fenway Park or playing golf at the Belmont Country Club.

BOSTON HEALTH LEAGUE

The annual meeting of the Boston Health League will be held at Perkins Hall, Women's Educational and Industrial Union, 264 Boylston Street, Boston, on Wednesday, April 23, at 12:30 p.m. Dr. G. Lynde Gately will speak on "Activities of the Health Department of the City of Boston."

The charge for luncheon will be 75 cents. Reservations, sent to the Boston Health League, Inc., 80 Federal Street, Boston, should be made by Monday, April 21.

MASSACHUSETTS GENERAL HOSPITAL

A meeting of the Hospital Research Council will be held in the Ether Dome of the Massachusetts General Hospital, on Tuesday, April 29, at 5 p.m.

PROGRAM

Observations on the Blocking Antibody in the Treatment of Hay Fever. Dr. Francis M. Rackemann and Miss Margaret Scully.
The Production of Hypothyroidism in Rabbits by the Injection of Thyroglobulin: Its relation to refractoriness. Dr. Jacob Lerman.
Roentgen Diagnosis of Primary Carcinoma of the Liver. Dr. Richard Schatzki.

MASSACHUSETTS SOCIETY FOR SOCIAL HYGIENE

The annual meeting of the Massachusetts Society for Social Hygiene will be held on Friday, April 25, at 4 p.m. in the Hotel Sheraton, 91 Bay State Road, Boston. The keynote of the program will be social hygiene and national defense. Brief reports will be given by Dr. George Gilbert Smith, president, and Mr. Richard H. Anthony, field representative in charge of the defense program of the society.

PROGRAM

The Soldier on Leave in Boston. Hon. Joseph Timilty, police commissioner of Boston.
Citizen Responsibility in National Defense from the Viewpoint of the Navy. Capt. Charles S. Stephenson, Bureau of Medicine and Surgery, Navy Department, Washington, D. C.

Following the program, tea will be served. The public is cordially invited to attend.

WALTHAM MEDICAL MEETING

There will be a clinicopathological staff conference of the Metropolitan State Hospital on Wednesday, April 30, at 8 p.m. A case of hemiplegia and aphasia will be presented by Drs. E. V. Semrad and R. C. Wadsworth. It will be discussed by Dr. Kurt Goldstein.

All interested physicians are cordially invited to attend.

ESSEX NORTH DISTRICT MEDICAL SOCIETY

The Essex North District Medical Society will celebrate its one hundredth anniversary on Wednesday, May 7, in Lawrence, Massachusetts. The centennial committee has prepared an interesting program for the day.

The annual business meeting of the district society will be followed by an inspection of hospitals of the city and a visit to the various textile plants. There will be a display of old photographs, instruments and manuscripts of historical significance in regard to the past one hundred years of the district society. The annual dinner will be held in the evening, at which time Dr. Walter G. Phippen, president of the Massachusetts Medical Society, and Dr. Frank H. Lahey, president-elect of the American Medical Association, will be the guest speakers. A group of fellows of the society, under the direction of Dr. Benjamin Spector, will present three dramatizations of important medical events that have occurred in the past one hundred years.

The ladies of the district have prepared an interesting afternoon for the wives of the members.

Essex North District Medical Society cordially invites members of the Massachusetts Medical Society to be present at this meeting. Reservations may be secured by writing to the secretary of the district, Dr. H. R. Kurth, 477 Essex Street, Lawrence.

WORCESTER NORTH DISTRICT MEDICAL SOCIETY

The eighty-second annual meeting of the Worcester North District Medical Society will be held at the Burbank Hospital, Fitchburg, on Wednesday, April 23.

PROGRAM

10:00 a.m. Gonadogen (medical film).
11:00 a.m. Treatment of General Peritonitis. Dr. Thomas J. Anglem, of the Massachusetts Memorial Hospitals.
11:30 a.m. Carcinoma of the Lung. Dr. John W. Strieder, of the Massachusetts Memorial Hospitals.
12:00 m. Recent Advances in Medical Therapy. Dr. Clifford L. Derick, of the Peter Bent Brigham Hospital.
12:30 p.m. Vitamin B Deficiency (medical film).
1:00 p.m. Recent Advances in Infant Feeding and Therapy. Dr. Edwin T. Wyman, of the Children's Hospital, Boston.
1:30 p.m. Indications for Cesarean Section. Dr. Joseph W. O'Connor, of the Worcester Memorial Hospital.
2:00 p.m. Dinner in the Nurses' Dining Room, Burbank Hospital.

UNITED STATES CIVIL SERVICE EXAMINATION

Psychiatric and Social Case Workers, $2000 a Year

There are now opportunities for social workers to enter governmental service as psychiatric or social case workers. Vacancies exist in the Veterans' Administration and in the Bureau of Prisons of the Department of Justice. An examination to fill these positions has been announced by the United States Civil Service Commission. The salary is $2000 a year.

Persons appointed in the Veterans' Administration will do psychiatric social work. In the hospitals and the regional offices of the Administration they will study patients' social needs to facilitate the medical diagnosis and treatment of the patients. Persons appointed in the Bureau of Prisons will act as social case workers in federal penal and correctional institutions. They will interview inmates and secure social data concerning them, and will co-operate with social agencies and federal probation officers on family needs and other factors affecting the inmates' adjustment. They will also follow through their duties by drafting plans for the inmates' release and subsequent readjustment.

A written test will not be given, but applicants must submit reports and writings as corroborative evidence of their training. They must have completed a four-year college course that included or was supplemented by one year of graduate or undergraduate study with a minimum of three hundred hours of supervised field work in an accredited school of social work. In addition, for positions in the Veterans' Administration, six semester hours' credit in psychiatric social work is required; and for positions in the Bureau of Prisons, six semester hours' credit in the methods of dealing with delinquent behavior.

Applications must be filed with the Commission's Washington office not later than May 14, 1941. Further information and application forms may be obtained at any first-class or second-class post office or from the Civil Service Commission.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING SUNDAY, APRIL 20

MONDAY, APRIL 21

American College of Physicians. Hotel Statler, Boston.

12:15–1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital amphitheater.

TUESDAY, APRIL 22

American College of Physicians. Hotel Statler, Boston.

12:15–1:15 p.m. Clinicoroentgenologic conference. Peter Bent Brigham Hospital amphitheater.

WEDNESDAY, APRIL 23

American College of Physicians. Hotel Statler, Boston.

*12 m. Clinicopathological conference. Children's Hospital.

12:30 p.m. Activities of the Health Department of the City of Boston. Dr. G. Lynde Gately. Boston Health League. Perkins Hall, Women's Educational and Industrial Union, 264 Boylston Street, Boston.

THURSDAY, APRIL 24

American College of Physicians. Hotel Statler, Boston.

FRIDAY, APRIL 25

American College of Physicians. Hotel Statler, Boston.

†4 p.m. Massachusetts Society for Social Hygiene. Hotel Sheraton, 91 Bay State Road, Boston.

8:15 p.m. Massachusetts Memorial Hospitals, staff meeting. Evans Memorial auditorium.

SATURDAY, APRIL 26

Boston City Hospital Alumni Day.

*Open to the medical profession.
†Open to the public.

APRIL 20 — Free public lecture, Quincy City Hospital. Page 436, issue of March 6.

APRIL 25 — Salem Tumor Clinic. Page 579, issue of March 27.

APRIL 28–30 — American Academy of Physical Medicine. Scientific session. Page 579, issue of March 27.

APRIL 29 — Massachusetts General Hospital. Page 708.

APRIL 30 — Boston Society of Biologists. Page 579, issue of March 27.

APRIL 30 — New England Pediatric Society. Page 671, issue of April 10.

APRIL 30 — Waltham Medical Meeting. Page 708.

MAY 5–9 — American Association of Industrial Physicians and Surgeons and American Industrial Hygiene Association. Page 484, issue of March 13.

MAY 8 — Pentucket Association of Physicians. Page 263, issue of August 15.

MAY 11 — Boston Doctors' Symphony Orchestra. Second annual concert. Page 671, issue of April 10.

MAY 12–14 — American Association for the Study of Goiter. Hotel Statler, Boston.

MAY 13–16 — National Gastroenterological Association. Hotel Commodore, New York City.

MAY 21, 22 — Massachusetts Medical Society, Boston.

MAY 28–JUNE 2 — American Board of Obstetrics and Gynecology. Page 262, issue of February 6.

MAY 29–31 — Medical Library Association. Page 671, issue of April 10.

MAY 30, 31 — American Heart Association. Hotel Statler, Cleveland.

MAY 30–JUNE 2 — American College of Chest Physicians. Hotel Statler, Cleveland.

JUNE 2–6 — American Medical Association. Cleveland.

OCTOBER 14–17 — American Public Health Association. Page 579, issue of March 27.

DISTRICT MEDICAL SOCIETIES

ESSEX NORTH

MAY 7 — Page 708.

ESSEX SOUTH

MAY 14 — Relation of the Doctor to the Law. Mr. Leland Powers. New Ocean House, Swampscott.

FRANKLIN

MAY 13 — This meeting will be held at 11 a.m. at the Franklin County Hospital, Greenfield.

NORFOLK
MAY 8 — Censors' meeting. Hotel Puritan, Boston.

SUFFOLK
APRIL 30 — Page 604, issue of October 10.
MAY 1 — Censors' meeting. Page 261, issue of February 6.

WORCESTER NORTH
APRIL 23 — Eighty-second annual meeting. Page 709.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Macleod's Physiology in Modern Medicine. Edited by Philip Bard, Ph.D., professor of physiology, Johns Hopkins University School of Medicine. With collaboration of Henry C. Bazett, M.D., L.R.C.P., professor of physiology, University of Pennsylvania; George R. Cowgill, Ph.D., associate professor of physiological chemistry, Yale University School of Medicine; Howard J. Curtis, Ph.D., instructor in physiology, Johns Hopkins University School of Medicine; Harry Eagle, M.D., lecturer in medicine, Johns Hopkins University School of Medicine; Chalmers L. Gemmill, M.D., associate in physiology, Johns Hopkins University School of Medicine; Magnus I. Gregersen, Ph.D., professor of physiology, College of Physicians and Surgeons, Columbia University; Roy G. Hoskins, Ph.D., M.D., director of research, Memorial Foundation for Neuroendocrine Research, and research associate in physiology, Harvard Medical School; J. M. D. Olmsted, Ph.D., professor of physiology, University of California; and Carl F. Schmidt, M.D., professor of pharmacology, University of Pennsylvania. Ninth edition. 8°, cloth, 1256 pp., with 124 tables and 387 illustrations. St. Louis: The C. V. Mosby Company, 1941. $10.00.

America Organizes Medicine. By Michael M. Davis, Ph.D., chairman, Committee on Research in Medical Economics. 8°, cloth, 335 pp. New York and London: Harper and Brothers, 1941. $3.00.

The Chemical Action of Ultraviolet Rays. By Carleton Ellis, B.S., and Alfred A. Wells. Revised and enlarged edition by Francis F. Heyroth, M.D., Ph.D., University of Cincinnati. 8°, cloth, 961 pp., with 159 illustrations. New York: Reinhold Publishing Corporation, 1941. $12.00.

Wolf Child and Human Child: Being a narrative interpretation of the life history of Kamala, the wolf girl. By Arnold Gesell, M.D., Yale University. 4°, cloth, 107 pp. New York: Harper and Brothers, 1941. $2.00.

Diseases Transmitted from Animals to Man. By Thomas G. Hull, Ph.D., director, The Scientific Exhibit, American Medical Association. Second edition. 8°, cloth, 403 pp., with 45 illustrations. Springfield, Illinois: Charles C Thomas, 1941. $5.50.

Hemorrhagic Diseases: Photo-electric study of blood coagulability. By Kaare K. Nygaard, M.D., fellow of the Alexander Malthe Foundation for Research in Medicine, Surgery and Gynecology. 8°, cloth, 320 pp., with 59 illustrations. St. Louis: The C. V. Mosby Company, 1941. $5.50.

The New International Clinics: Original contributions, clinics, and evaluated reviews of current advances in the medical arts. Edited by George Morris Piersol, M.D., professor of medicine, Graduate School of Medicine, University of Pennsylvania, Philadelphia. Vol. 1, N. S. 4, 1941. 8°, cloth, 304 pp., with 44 illustrations, and 19 tables. Philadelphia: J. B. Lippincott Company, 1941. $3.00.

Manual of Clinical Chemistry. By Miriam Reiner, M.Sc., assistant chemist, Mount Sinai Hospital, New York. Introduction by Harry Sobotka, Ph.D., chemist, Mount Sinai Hospital. 12°, cloth, 296 pp. New York: Interscience Publishers, Incorporated, 1941. $3.00.

An Introduction to Dermatology. By Richard L. Sutton, M.D., Sc.D., LL.D., F.R.S. (Edin.), emeritus professor of dermatology, University of Kansas School of Medicine; and Richard L. Sutton, Jr., M.D., L.R.C.P. (Edin.), assistant professor of dermatology, University of Kansas School of Medicine. Fourth edition. 8°, cloth, 904 pp., with 723 illustrations. St. Louis: The C. V. Mosby Company, 1941. $9.00.

American Gynecological Society Transactions. Vol. 65 (1940). Edited by Richard W. TeLinde, M.D. 8°, cloth, 241 pp., with 77 figures and 73 tables. St. Louis: The C. V. Mosby Company, 1941.

Spermatozoa and Sterility: A clinical manual. By Abner I. Weisman, M.D., adjunct gynecologist, Jewish Memorial Hospital, and clinical assistant visiting gynecologist and obstetrician, Metropolitan Hospital, New York. With a foreword by Robert L. Dickinson, M.D. 8°, cloth, 314 pp., with 70 illustrations. New York: Paul B. Hoeber, Incorporated, 1941. $5.50.

Blood Transfusion Association: Report concerning the project for supplying blood plasma to England. Narrative account of work and medical report. 8°, paper, 21 pp. New York: Blood Transfusion Association, 1941.

Surgery of Modern Warfare. Vol. I. By sixty-five contributors. Edited by Hamilton Bailey, F.R.C.S.; surgeon, Royal Northern Hospital, London. 4°, cloth, 480 pp., with 502 illustrations. Baltimore: Williams and Wilkins Company, 1941. $10.00.

BOOK REVIEW

The Chinese Way in Medicine. By Edward H. Hume, M.D. 8°, cloth, 189 pp., with 8 illustrations. Baltimore: Johns Hopkins Press, 1940. $2.25.

This stimulating little volume seeks to place before the reader a rapid survey of a system of medical thought that is philosophical in conception and has proved adequate for the needs of an eastern Asiatic civilization.

The three lectures that form the basis for this book are: "The Universe and Man in Chinese Medicine," "The Founders and Chief Exemplars of Chinese Medicine" and "Some Distinctive Contributions of Chinese Medicine." The author develops in an admirable manner the three characteristic approaches of the Chinese way in medicine — the cosmic, the animistic and the medicamental. The thesis is presented that the Chinese have made significant contributions in the fields of medical literature, medicaments, physical therapy and diagnostic methods. Although this book may make its appeal to a strictly professional group, it is to be highly recommended to students in colleges of liberal arts, as well as to those in medical schools.